OM of: US-09-303-518D-651 to: A_Geneseq_032802:* out_format : pfs

Date: Jun 30, 2002 7:01 AM

About: Results were produced by the GenCore software, version 4.5,
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Command line parameters:
-MODEL=frame+_n2p.model -DEV=x1h
-Q=/cgn2_1/USPTO_spool/US09303518/runat_28062002_142712_4291/app_query.fasta_1.23501
-DB=A_Geneseq_032802 -QFMT=fastan -SUFFIX=rag -GAPOP=12.000
-GAPEXT=4.000 -MINMATCH=0.100 -LOOPCL=0.000 -LOOPEXT=0.000
-QGAPOP=4.500 -QGAPEXT=0.050 -XGAPOP=10.000 -XGAPEXT=0.500
-FGAPOP=6.000 -FGAPEXT=7.000 -YGAPOP=10.000 -YGAPEXT=0.500
-DELOP=6.000 -DELEXT=7.000 -START=1 -MATRIX=blosum62
-TRANS=human40.cdi -LIST=100 -DOCALIGN=200 -THR_SCORE=pct
-THR_MAX=100 -THR_MIN=0 -ALIGN=45 -MODE=LOCAL -OUTFMT=pfs
-NORM=ext -HEAPSIZE=500 -MINLEN=0 -MAXLEN=2000000000
-USER=US09303518_@CGN1_1_0 -NCPU=6 -ICPU=3 -LONGLOG
-DEV_TIMEOUT=120 -WARN_TIMEOUT=30 -NO_XLPXY -WAIT -THREADS=1

Search information block:
Query: US-09-303-518D-651
Query length: 4350
Database: A_Geneseq_032802:*
Database sequences: 747574
Database length: 111073796
Search time (sec): 627.340000

score_list:

Sequence	Strd	Orig	ZScore	EScore	Len	! Documentation ..			
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/SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:ABB52745	+	1056.50	1399.46	6.1e-71	13				
/SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:ABB52592	+	1038.00	1374.41	1.5e-69	13				
/SIDS1/gcgdata/geneseq/geneseqp-embl/AA1997.DAT:AAW27705	+	709.50	945.68	4.9e-45	32				
/SIDS1/gcgdata/geneseq/geneseqp-embl/AA1988.DAT:AAP80136	+	385.50	498.91	1.6e-20	74				
/SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:AAG98842	+	372.50	473.40	2.0e-19	15				
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seq_documentation_block:
ID AAR07304 standard; protein; 1541 AA.
XX
AC AAR07304;
XX
DT 31-JAN-1991 (first entry)
XX
DE IgA1 protease.
XX
KW IgA1; vaccine; meningitis; gonnorhoea; allergies.
XX
OS Haemophilus influenzae.
XX
PN WO9011367-A.
XX
PD 04-OCT-1990.
XX
PF 16-MAR-1990; 90WO-DK00073.
XX
PR 17-MAR-1989; 89DK-0001308.
XX

```
PA   (KILI/) KILIAN M.
XX
PI   Kilian M,  Poulsen K;
XX
DR   WPI; 1990-320267/42.
DR   N-PSDB; AAQ06164.
XX
PT   Immunoglobulin A1 protease prodn. - by cloning from
PT   microorganisms for immunisation against immunoglobulin A1
PT   protease producing bacteria
XX
PS   Disclosure; fig 3; 44pp; English.
XX
CC   This immunoglobulin (Ig)A1 protease is produced by recombinant DNA
CC   methods.  It is useful in a vaccine for e.g. meningococcal meningitis,
CC   gonorrhoea or allergic diseases.  It specifically cleaves the heavy
CC   chain of human IgA1 in the hinge region.
XX
SQ   Sequence   1541 AA;
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alignment_scores:
Quality: 1536.50 Length: 1722
Ratio: 1.677 Gaps: 56
Percent Similarity: 53.194 Percent Identity: 26.887

alignment_block:
US-09-303-518D-651 x AAR07304 ..

Align seg 1/1 to: AAR07304 from: 1 to: 1541

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      5 LysPheLysLeuAsnPheIleAlaLeuThrValAlaTyrAlaLeuThrPr 21

    114 CCAAGCTTGGGCGGGACACACTTATTTCGGCATCAACTACCAATACTATC 163
        |   :::   |||:::   :::         ::::::||||||   :::|
     21 oTyrThrGluAlaAlaLeuValArgAspAspValAspTyrGlnIlePheA 38

    164 GCGACTTTGCCGAAAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATT 213
        ||||||||||||||||||||||||||||::||||||||   ::::::
     38 rgAspPheAlaGluAsnLysGlyLysPheSerValGlyAlaThrAsnVal 54

    214 GAGGTNTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGC 263
           |||   :::|||:::::::::   :::|||   ::::::   :::::
     55 LeuValLysAspLysAsnAsnLysAspLeuGlyThrAlaLeuProAsnGl 71

    264 C...CCGATGATTGATTTTTCTGTGGTGTCG...CGTAACGGCGTGGCGG 307
        :  ||||||||||||||||||||||:::      :::   :::|||:
     71 yIleProMetIleAspPheSerValValAspValAspLysArgIleAlaT 88

    308 CATTGGTGGGCGATCAATATATTGTGAGCGTGGCACAT...AACGGCGGC 354
        ::|||::::::   ||||||:::|||:::|||   |||   ::::::|||
     88 hrLeuIleAsnProGlnTyrValValGlyValLysHisValSerAsnGly. 104

    355 TATAACAACGTTGATTTTGGT.............GCGGAAGGAAGNAA 389
           :::::::::   ||||||                  ::::::   ||
    105 ValSerGluLeuHisPheGlyAsnLeuAsnGlyAsnMetAsnAsnGlyAs 121

    390 TCCCGATCAGCACCGT.................TTTTCTTACCAAATTG 421
        |   |||||                                |||     |
    121 nAlaLysAlaHisArgAspValSerSerGluGluAsnArgTyrPheSerV 138

    422 TGAAAAGAAATAATTAT.............................AAG 441
        ||:::::|||:::|||
    138 alGluLysAsnGluTyrProThrLysLeuAsnGlyLysThrValThrThr 154

    442 CCTGACAATTCACACCCTTACAACGGCGATTANCATATGCCGCGTTTGCA 491
           |||:::::::::      :::   |||   :::|||||||||||||
    155 GluAspGlnThrGlnLysArgArgGluAspTyrTyrMetProArgLeuAs 171

    492 TAAATTTGTCACAGATGCAGAACCTGTCGAA...ATGACGAGTGACATGA 538
         ||||||||||||:::::   |||:::|||      |||::::::
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    171 pLysPheValThrGluValAlaProIleGluAlaSerThrAlaSerSerA 188

    539 GGGGGAATACCTATTCCGATAAAGAAAAATATCCCGAGCGTGTCCGCATC 588
          :::::|||||:::|||:::::|||||||||      ||||||:::
    188 spAlaGlyThrTyrAsnAspGlnAsnLysTyrProAlaPheValArgLeu 204

    589 GGCTCAGGACACCACTATTGGCGTTATGATGATGACAAACACGGCGATTT 638
        |||||||||   :::::                  |||   ||||||
    205 GlySerGlySerGlnPheIleTyr...........LysLysGlyAsp.. 216

    639 ATCCTACTCCGGCGCATGGTTAATTGGCGGCAATACACATATGCAGGGTT 688
         :::||||||            :::      |||:::|||      |||
    217 .AsnTyrSer............LeuIleLeuAsnAsnHisGluValGly. 228

    689 GGGGAAATAAT............................GGCGTANTT 708
          |||||||||                            |||::::::
    229 ..GlyAsnAsnLeuLysLeuValGlyAspAlaTyrThrTyrGlyIleAla 244

    709 AGTTTGAGCGGCGATGTGCGCCATGCCAACGAC............TATGG 746
        :::           |||:::|||   |||:::         :::||
    245 GlyThrProTyrLysValAsnHisGluAsnAsnGlyLeuIleGlyPheGl 261

    747 C.............................................C 748
        |                                             |
    261 yAsnSerLysGluGluHisSerAspProLysGlyIleLeuSerGlnAspP 278

    749 CTATGCCGATTGCAGGTGCGGCAGGCGACAGCGGTTCGCCAATGTTTATT 798
        ||:::         :::::   |||||||||||||||||:::|||:::
    278 roLeuThrAsnTyrAlaValLeuGlyAspSerGlySerProLeuPheVal 294

    799 TATGACAAAACAAACAATAAATGGCTGCTCAACGGAGTTTTACAAACCGG 848
        ||||||:::   ::::::||||||||||:::   |||            ::
    295 TyrAspArgGluLysGlyLysTrpLeuPheLeuGly............Se 307

    849 CTACCCTTATTCCGGCAGGGAAAACGGTTTCCAGCTGATACGCAAAGATT 898
        :|||   :::   :::      |||                ::::|||:::|
    307 rTyrAspPheTrpAlaGlyTyrAsn..............LysLysSerT 319

    899 GGTTCTACGATGACATTTACAGAGGCGATACACATACCGTCTNTTTTGAA 948
        ||         :::||||||::::::
    319 rpGlnGluTrpAsnIleTyrLysSer....................... 327

    949 CCGCGCAGTAACGGACATTTTTCCTTTACATCC.........AACAACAA 989
                              :::|||||||:::          |||:::::
    328 .....................GlnPheThrLysAspValLeuAsnLysAs 337

    990 CGGTACGGGTACGGTAACAGAAACCAACGAAAAGGTNTCC...AATCCAA 1036
        :::::::|||::::::      ::::::          |||   :::   :
    337 pSerAlaGlySerLeuIleGlySerLysThrAspTyrSerTrpSerSerA 354

   1037 AGCTTAAAGTACAGACAGTCCGACTGTTTGACGAATCTTTGAATGAAACT 1086
        ::   |||:::::::|||:::          ::::::|||||||||
    354 snGlyLysThrSerThrIleThrGlyGlyGluLysSerLeuAsn..... 368

   1087 GATAAAGAACCAGTTTACGCGGCAGGGGGTGTTAATCAGTACCGTCCAAG 1136
                  |||      |||   |||            :::   ::
    369 ............ValAspLeuAlaAspGly............LysAspLy 377

   1137 GTTAAACAACGGTGAAAACCTTTCTTTTATCGATTACGGCAACGGCAAAC 1186
        :   |||:::|||:::::::::::::|||          |||:::|||   |
    377 sProAsnHisGlyLysSerValThrPhe.....GluGlySerGlyThrL 392

   1187 TCATCTTATCAAACAACATCAACCAAGGCGCGGGCGGTTTGTATTTTGAA 1236
        ||   |||:::||||||||||:::|||||||||||||||||||:::||||||
    392 euThrLeuAsnAsnAsnIleAspGlnGlyAlaGlyGlyLeuPhePheGlu 408

   1237 GGTGATTTTACGGTC...TCGCCTGAAAACAACGAAACGTGGCAAGGCGC 1283
        |||||||:::   |||   :::   :::::|||   ||||||:::||||
    409 GlyAspTyrGluValLysGlyThrSerAspAsnThrThrTrpLysGlyAl 425

   1284 GGGCGTTCATATCAGTGAAGACAGTACCGTTACTTGGAAAGTAAACGGCG 1333
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    425 aGlyValSerValAlaGluGlyLysThrValThrTrpLysValHisAsnP 442
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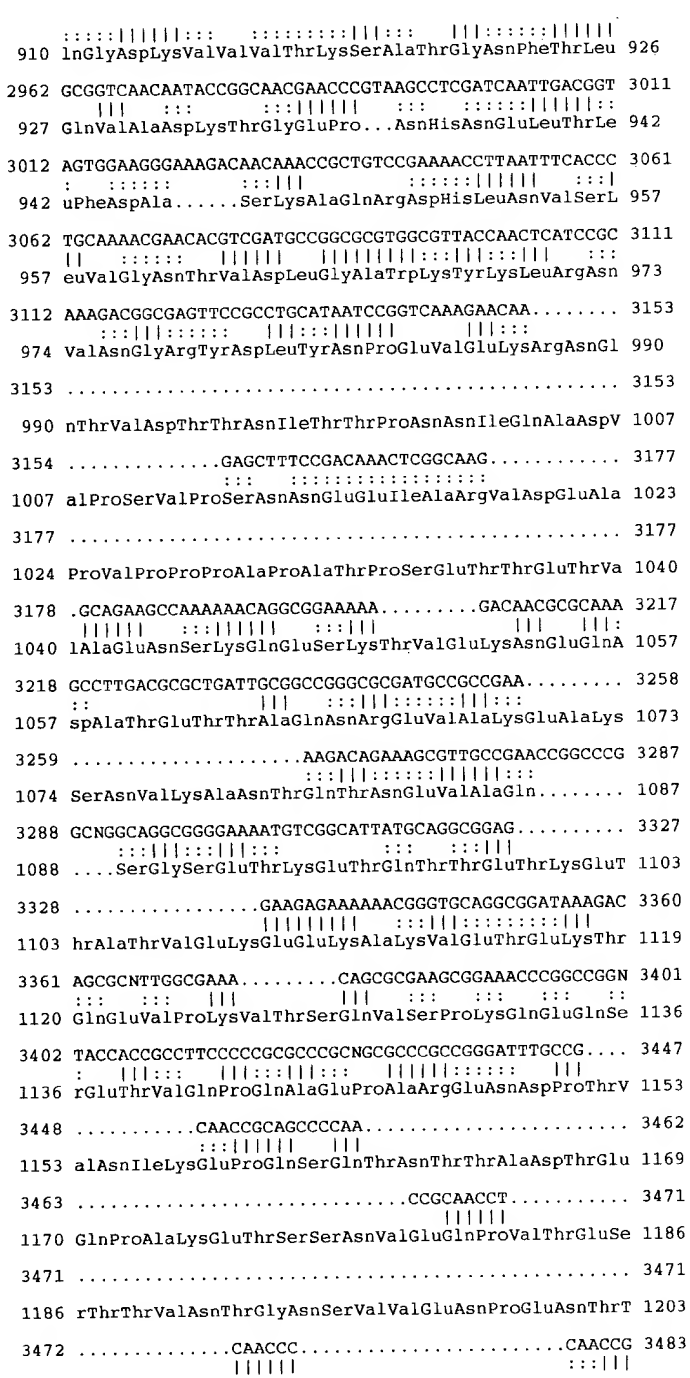
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927 GlnValAlaAspLysThrGlyGluPro...AsnHisAsnGluLeuThrLe 942
3012 AGTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCACCC 3061
942 uPheAspAla.....SerLysAlaGlnArgAspHisLeuAsnValSerL 957
3062 TGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACTCATCCGC 3111
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3153 3153
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3218 GCCTTGACGCGCTGATTGCGGCCGGGCGCGATGCCGCCGAA..... 3258
1057 spAlaThrGluThrThrAlaGlnAsnArgGluValAlaLysGluAlaLys 1073
3259 .....AAGACAGAAAGCGTTGCCGAACCGGCCCG 3287
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1088 ....SerGlySerGluThrLysGluThrGlnThrThrGluThrLysGluT 1103
3328 .....GAAGAGAAAAAACGGGTGCAGGCGGATAAAGAC 3360
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1120 GlnGluValProLysValThrSerGlnValSerProLysGlnGluGlnSe 1136
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3448 .....CAACCGCAGCCCCAA..... 3462
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1484 sIleAsnValAsnGlyTyrAspPheAlaTyrAsnValGluAsnGlnGlnG 1501
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DT   21-MAR-2000  (first entry)
XX
DE   Neisseria meningitidis ORF 759 protein sequence SEQ ID NO:2602.
XX
KW   Neisseria meningitidis; Neisseria gonorrheae; antigen; vaccine;
KW   antigenic; diagnosis; immunogenic; infection; meningitis; septicaemia;
KW   antibacterial; gene therapy.
XX
OS   Neisseria meningitidis.
XX
PN   WO9957280-A2.
XX
PD   11-NOV-1999.
XX
PF   30-APR-1999;   99WO-US09346.
XX
PR   01-MAY-1998;   98US-0083758.
PR   31-JUL-1998;   98US-0094869.
PR   02-SEP-1998;   98US-0098994.
PR   02-SEP-1998;   98US-0099062.
PR   09-OCT-1998;   98US-0103749.
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PR   25-FEB-1999;   99US-0121528.
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DR   WPI; 2000-062150/05.
DR   N-PSDB; AAZ54326.
XX
PT   Novel Neisserial polypeptides predicted to be useful antigens for
PT   vaccines and diagnostics  -
XX
PS   Claim 2; Page 1234; 1453pp; English.
XX
CC   AAZ53015 to AAZ54536, AAZ54577 to AAZ54615, and AAY74253 to AAY75941
CC   represent novel Neisseria meningitis and N. gonorrheae polynucleotides
CC   and polypeptides. AAZ54537 to AAZ54576 and AAZ54616 to AAZ55473 represent
CC   PCR primers used in the exemplification of the present invention. The
CC   polypeptides, the polynucleotides, antibodies and compositions of
CC   the invention can be used as vaccines, as diagnostic reagents, and as
CC   immunogenic compositions. The polypeptides can be used in the
CC   manufacture of medicaments for treating or preventing infection due to
CC   Neisserial bacteria (e.g. meningitis and septicaemia), to detect the
CC   presence of Neisseria bacteria, or to raise antibodies. They may also
CC   be used to screen for agonists or antagonists, which may themselves
CC   have use as antibacterial agents. The polynucleotides of the invention
CC   may also be used in gene therapy protocols.
XX
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     532 .GACATGAGGGGGAATACCTATTCCGATAAAGAAAAATATCCCGAGCGTG 580
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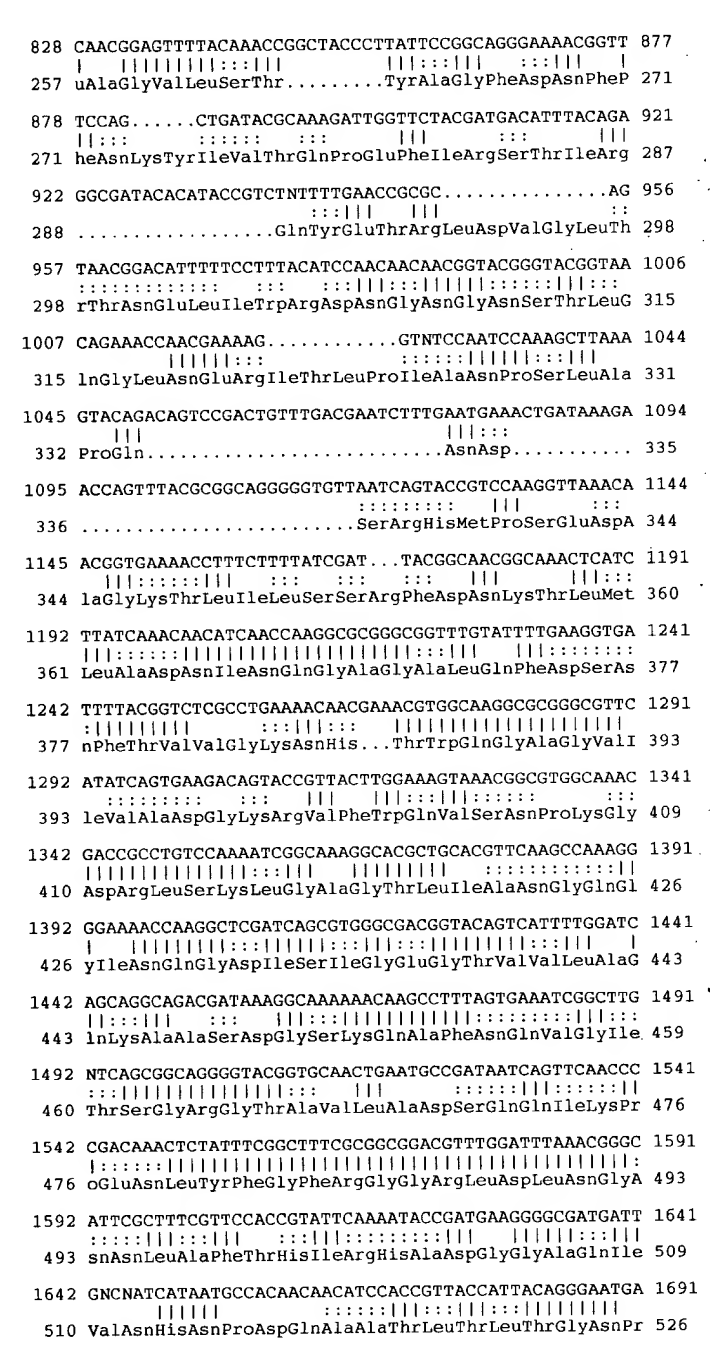
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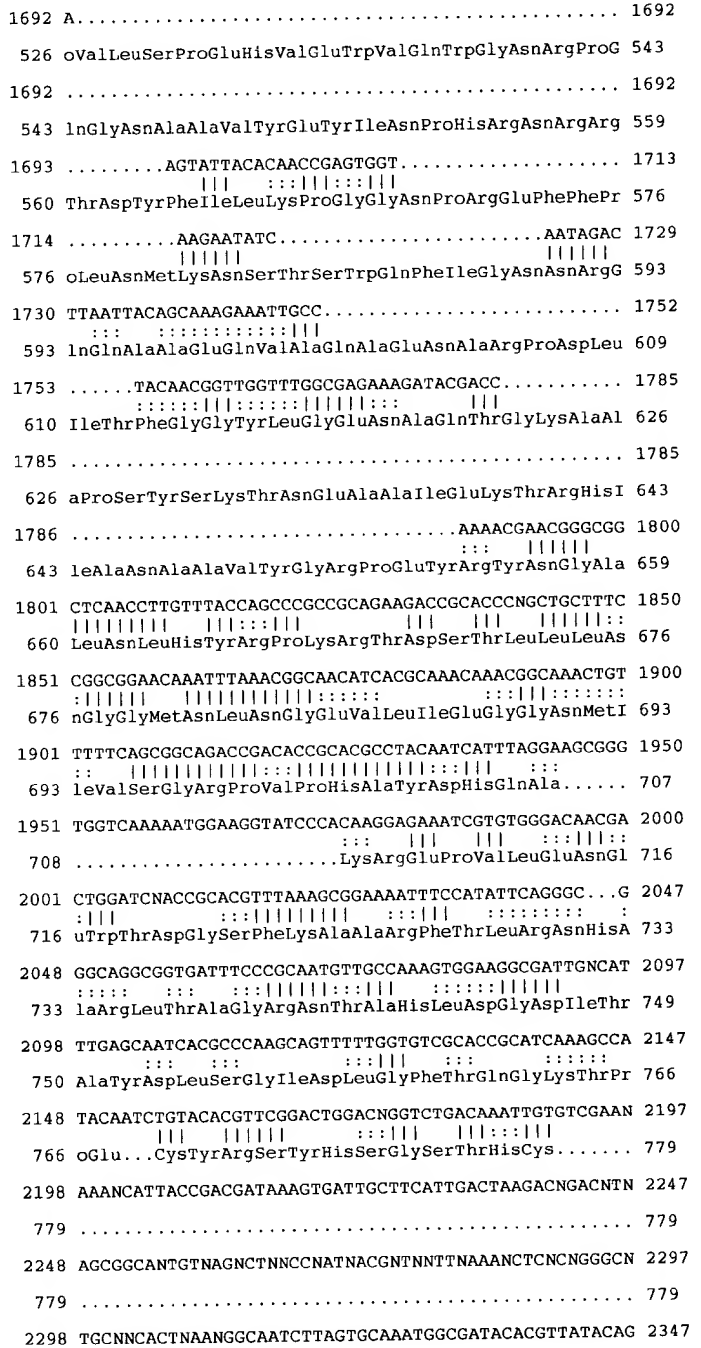
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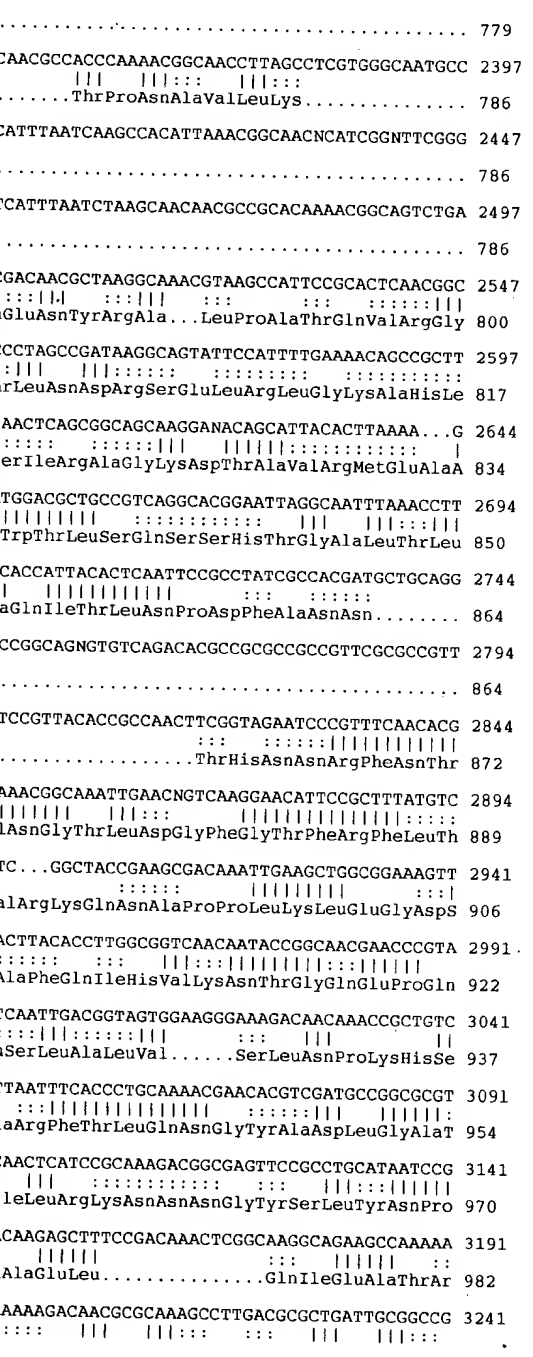

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XX
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KW immunosuppressive; extra-intestinal infection; phylogeny; meningitis;
KW systemic infection; non-diarrhoeal infection; septicaemia;
KW pyelonephritis; antibiotic resistance.
XX
OS Escherichia coli.
XX
PN WO200166572-A2.
XX
PD 13-SEP-2001.
XX
PF 12-MAR-2001; 2001WO-EP03445.
XX
PR 10-MAR-2000; 2000FR-0003145.
PR 02-FEB-2001; 2001FR-0001449.
XX
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XX
PI Bingen E, Bonacorsi S, Clermont O, Nassif X, Tinsley C;
XX
DR WPI; 2001-550253/61.
XX
PT A library of DNA fragments of Escherichia coli strains for the
PT phylogenic determination of a given strain comprises polynucleotides of
PT nature B2/D+ A- -
XX
PS Example 6; Fig 6; 646pp; English.
XX
CC The invention relates to a library of DNA fragments of Escherichia coli
CC strains comprising polynucleotides (ABA88577-ABA88729 and ABA89533)
CC and encoded proteins (ABB52459-ABB52919 and ABB52954-ABB53094) of nature
CC B2/D+A-. The polynucleotides have potential antiinflammatory,
CC antibacterial and immunosuppressive activity as part of pharmaceutical
CC compositions used to treat, palliate or prevent extra-intestinal E. coli
CC infections. The polypeptides are useful for determining the phylogenic
CC group of a given E. coli strain. These polypeptides can detect and treat
CC an undesired development of E. coli, particularly an extra-intestinal
CC infection that include systemic and non-diarrhoeal infections such as
CC septicaemia, pyelonephritis and meningitis this is particularly
CC advantageous as bacterial resistance is increasing with the more
CC frequent use of broad spectrum antibiotics.
XX
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Ratio:	1.360	Gaps:	65
Percent Similarity:	49.427	Percent Identity:	26.272

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 409 TCTTACCAAATTGTGAAAAGAAATAATTATAAGCCTGACAATTCACACCC 458
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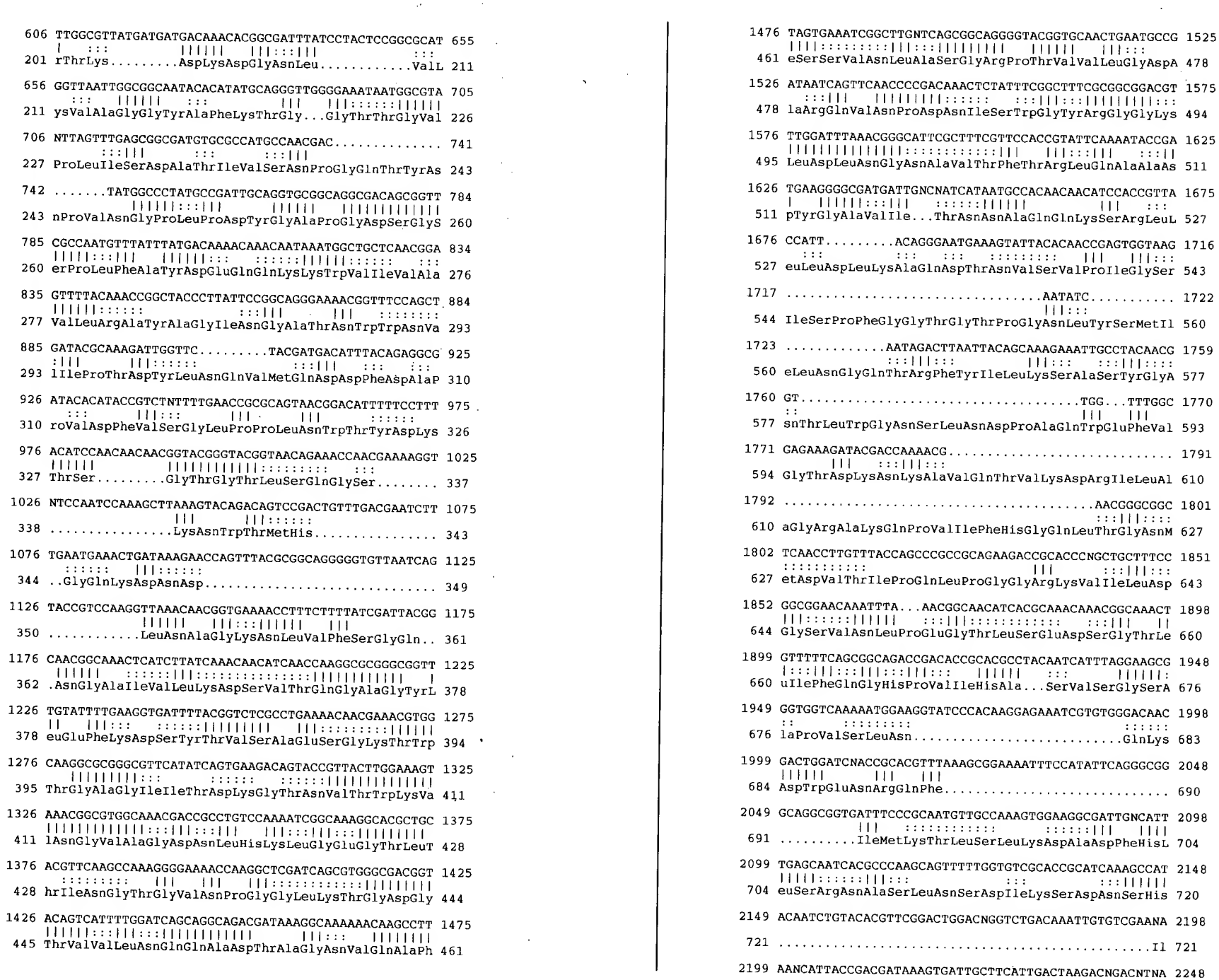

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DT   11-FEB-2002  (first entry)
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DE   Escherichia coli polypeptide SEQ ID NO 560.
XX
KW   Escherichia coli; B2/D+A-; antiinflammatory; antibacterial;
KW   immunosuppressive; extra-intestinal infection; phylogeny; meningitis;
KW   systemic infection; non-diarrhoeal infection; septicaemia;
KW   pyelonephritis; antibiotic resistance.
XX
OS   Escherichia coli.
XX
PN   WO200166572-A2.
XX
PD   13-SEP-2001.
XX
PF   12-MAR-2001; 2001WO-EP03445.
XX
PR   10-MAR-2000; 2000FR-0003145.
PR   02-FEB-2001; 2001FR-0001449.
XX
PA   (INRM ) INSERM INST NAT SANTE & RECH MEDICALE.
XX
PI   Bingen E,  Bonacorsi S,  Clermont O,  Nassif X,  Tinsley C;
XX
DR   WPI; 2001-550253/61.
XX
PT   A library of DNA fragments of Escherichia coli strains for the
PT   phylogenic determination of a given strain comprises polynucleotides of
PT   nature B2/D+ A- -
XX
PS   Example 6; Fig 6; 646pp; English.
XX
CC   The invention relates to a library of DNA fragments of Escherichia coli
CC   strains comprising polynucleotides (ABA88577-ABA88729 and ABA89533)
CC   and encoded proteins (ABB52459-ABB52919 and ABB52954-ABB53094) of nature
CC   B2/D+A-. The polynucleotides have potential antiinflammatory,
CC   antibacterial and immunosuppressive activity as part of pharmaceutical
CC   compositions used to treat, palliate or prevent extra-intestinal E. coli
CC   infections. The polypeptides are useful for determining the phylogenic
CC   group of a given E. coli strain. These polypeptides can detect and treat
CC   an undesired development of E. coli, particularly an extra-intestinal
CC   infection that include systemic and non-diarrhoeal infections such as
CC   septicaemia, pyelonephritis and meningitis this is particularly
CC   advantageous as bacterial resistance is increasing with the more
CC   frequent use of broad spectrum antibiotics.
XX
SQ   Sequence   1376 AA;
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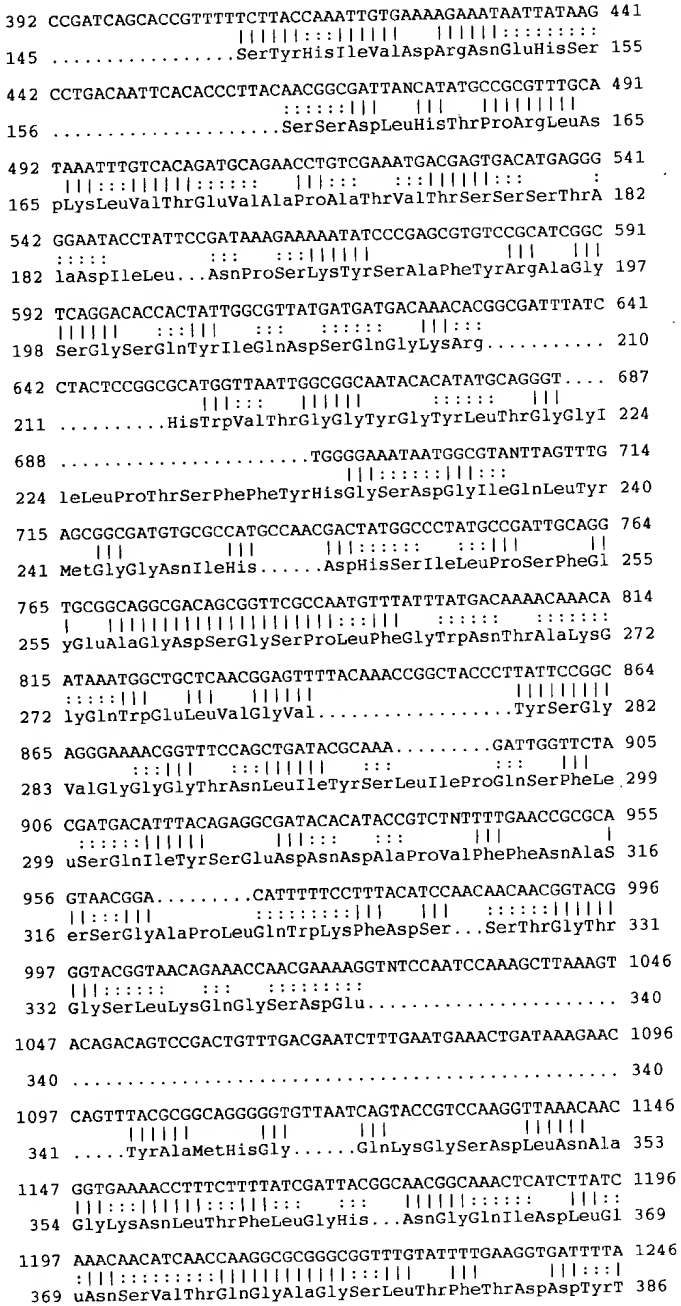
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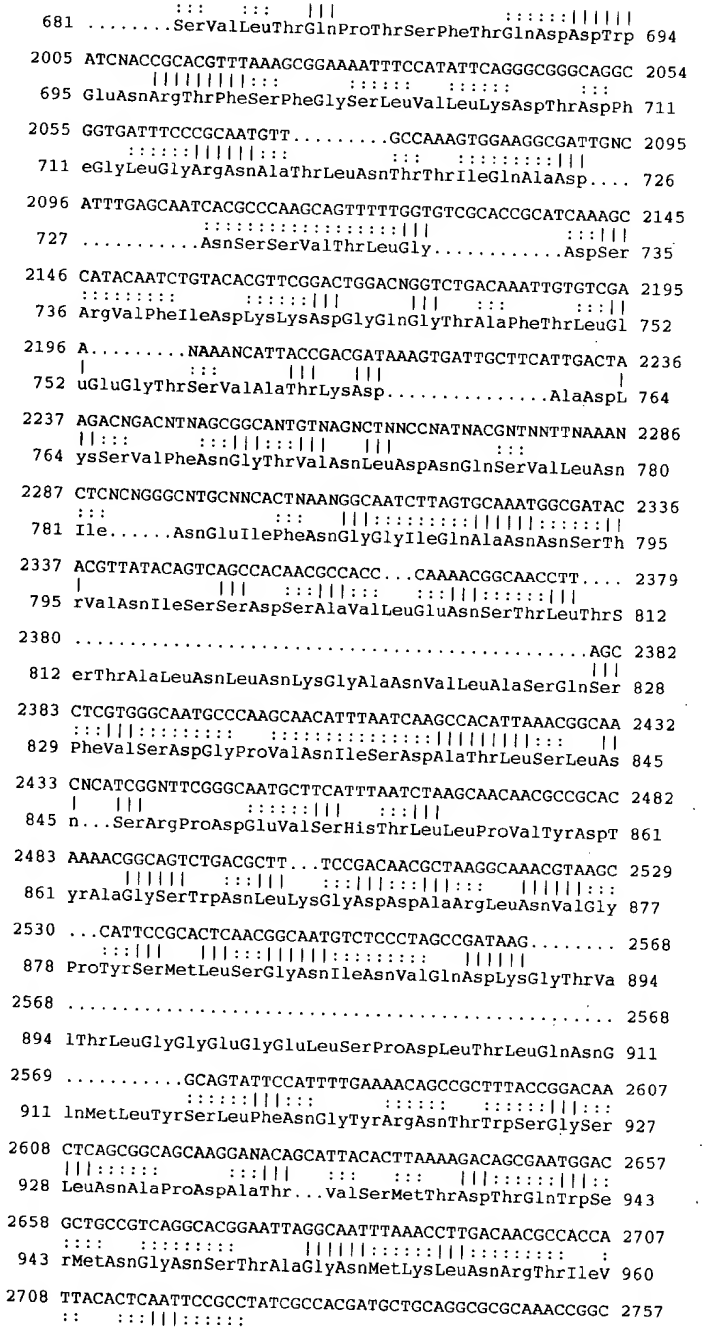
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764 ysSerValPheAsnGlyThrValAsnLeuAspAsnGlnSerValLeuAsn 780
2287 CTCNCNGGGCNTGCNNCACTNAANGGCAATCTTAGTGCAAATGGCGATAC 2336
781 Ile.....AsnGluIlePheAsnGlyGlyIleGlnAlaAsnAsnSerTh 795
2337 ACGTTATACAGTCAGCCACAACGCCACC...CAAAACGGCAACCTT.... 2379
795 rValAsnIleSerSerAspSerAlaValLeuGluAsnSerThrLeuThrS 812
2380 .....AGC 2382
812 erThrAlaLeuAsnLeuAsnLysGlyAlaAsnValLeuAlaSerGlnSer 828
2383 CTCGTGGGCAATGCCCAAGCAACATTTAATCAAGCCACATTAAACGGCAA 2432
829 PheValSerAspGlyProValAsnIleSerAspAlaThrLeuSerLeuAs 845
2433 CNCATCGGNTTCGGGCAATGCTTCATTTAATCTAAGCAACAACGCCGCAC 2482
845 n...SerArgProAspGluValSerHisThrLeuLeuProValTyrAspT 861
2483 AAAACGGCAGTCTGACGCTT...TCCGACAACGCTAAGGCAAACGTAAGC 2529
861 yrAlaGlySerTrpAsnLeuLysGlyAspAspAlaArgLeuAsnValGly 877
2530 ...CATTCCGCACTCAACGGCAATGTCTCCCTAGCCGATAAG..... 2568
878 ProTyrSerMetLeuSerGlyAsnIleAsnValGlnAspLysGlyThrVa 894
2568 2568
894 lThrLeuGlyGlyGluGlyGluLeuSerProAspLeuThrLeuGlnAsnG 911
2569 .....GCAGTATTCCATTTTGAAAACAGCCGCTTTACCGGACAA 2607
911 lnMetLeuTyrSerLeuPheAsnGlyTyrArgAsnThrTrpSerGlySer 927
2608 CTCAGCGGCAGCAAGGANACAGCATTACACTTAAAAGACAGCGAATGGAC 2657
928 LeuAsnAlaProAspAlaThr...ValSerMetThrAspThrGlnTrpSe 943
2658 GCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTGACAACGCCACCA 2707
943 rMetAsnGlyAsnSerThrAlaGlyAsnMetLysLeuAsnArgThrIleV 960
2708 TTACACTCAATTCCGCCTATCGCCACGATGCTGCAGGCGCGCAAACCGGC 2757
960 alGlyPheAsnGlyGly..... 965
2758 AGNGTGTCAGACACGCCGCGCCGCCGTTCGCGCCGTTCCCTATTATCCGT 2807
965 965
2808 TACACCGCCAACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACG 2857
966 .....ThrSerSerPheThrThrLeuThrThrAspA 976
2858 GCAAATTGAACNGTCAAGGAACATTCCGCTTTATGTCGGAACTCTTCGGC 2907
976 snLeuAspAlaValGlnSerAlaPheValMetArgThrAspLeu..... 990
2908 TACCGAAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGNACTTACAC 2957
991 AsnLysAlaAspLysLeuValIleAsnLysSerAlaThrGlyHisAspAs 1007
2958 CTTGGCGGTCAACAATACCGGCAACGAACCCGTAAGCCTCGATCAATTGA 3007
1007 nSerIleTrpValAsnPheLeuLysLysProSerAspLysAspThrLeuA 1024
3008 CGGTAGTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTT..... 3051
1024 spIleProLeuValSerAlaProGluAlaThrAlaAspAsnLeuPheArg 1040
3052 .....AATTTCACCCTGCAAAA 3068
1041 AlaSerThrArgValValGlyPheSerAspValThrProThrLeuServa 1057
3069 CGAACACGTCGATGCC...GGCGCGTGG.....CGTTACCAACTCA 3106
1057 lArgLysGluAspGlyLysLysGluTrpValLeuAspGlyTyrGlnValA 1074
3107 TCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAG 3156
1074 laArgAsnAspGlyGln..... 1079
3157 CTTTCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGA 3206
1080 .....GlyLysAlaAlaAlaThrPheMetHisIleSerTy 1091
3207 CAAC.....GCGCAAAGCCTTGACGCGCTGATTGCGGCCG 3241
1091 rAsnAsnPheIleThrGluValAsnAsnLeuAsnLysArgMetGlyAspL 1108
3242 GGCGCGATGCCGCCGAAAAGACAGAAAGCGTTGCCGAACCGGCCCGGCNG 3291
1108 euArgAspIleAsnGlyGluAlaGlyThrTrpValArgLeuLeuAsnGly 1124
3292 GCAGGCGGGGAAAATGTCGGC.....ATTATGCAGGC 3323
1125 SerGlySerAlaAspGlyGlyPheThrAspHisTyrThrLeuLeuGlnMe 1141
3324 GGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGAC..... 3360
1141 tGlyAlaAspArgLysHisGluLeuGlySerMetAspLeuPheThrGlyV 1158
3361 .....AGCGCNTTGGCGAAACAGCGCGAAGCG 3387
1158 alMetAlaThrTyrThrAspThrAspAlaSerAlaGlyLeuTyrSerGly 1174
3388 GAAACCCGGCCGGNTACCACCGCCTTCCCCCGCGCCCGCNGCGCCCGCCG 3437
1175 LysThrLysSerTrpGlyGlyGlyPheTyrAlaSerGlyLeuPheArgSe 1191
3438 GGATTTGCCGCAACCGCAGCCCCAACCGCAACCTCAACCCCAACCGCAGC 3487
1191 rGly.....AlaTyrP 1195
3488 GCGACCTGATNAGCCGTTAT..... 3507
1195 heAspLeuIleAlaLysTyrIleHisAsnGluAsnLysTyrAspLeuAsn 1211

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  3508 ...GCCAATAGCGGTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTTTT 3554
       |||::::::|||   :::::::|||   :::      :::|||::::: 
  1212 PheAlaGlyAlaGlyLysGlnAsnPheArgSer.....HisSerLeuTy 1226

  3555 CGCCGTACAGGACGAA.................TTGGACCGCGTGTTTG 3586
       :|||      :::                    |||   :::|||: 
  1226 rAlaGlyAlaGluValGlyTyrArgTyrHisLeuThrAspThrThrPheV 1243

  3587 CCGAAGACCGCCGCAACGCNGTTTGGACAAGCNGCATCCGGNACACCAAA 3636
       ::|||   :::   :::   ||||||                  |||
  1243 alGluProGlnAlaGluLeuValTrpGlyArgLeuGlnGlyGlnThrPhe 1259

  3637 CACTACCGTTCGCAAGATTTCCGCGCCTACCGCCAACAAACCGACCTGCG 3686
       ::::::::::::::   :::
  1260 AsnTrpAsnAspSerGlyMet........................... 1266

  3687 CCAAATCGGTATGCAGAAAAACCTCGGCAGC.........GGGCGCGTCG 3727
        :::::::::|||::::::|||      :::          |||||||:::|
  1267 .AspValSerMetArgArgAsnSerValAsnProLeuValGlyArgThrG 1283

  3728 GCATCCTGTTTTCGCACAACCGGACCGAAAACANCTTCGACGACGGCATC 3777
       ||::::::         :::::::|||   :::      |||   ::::::
  1283 lyValVal......SerGlyLysThrPheSerGlyLysAspTrpSerLeu 1297

  3778 GGCAACTCGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAATACGGCAT 3827
               |||   |||   :::
  1298 ThrAlaArgAlaGlyLeuHisTyr.......................... 1305

  3828 CGGCAGGTTCGACATCGGCATCAGCACGGGCGCGGGTTTTAGCAGCGGCA 3877
       :::||||||:::      |||:::   :::   :::::::::::::
  1306 ....GluPheAspLeuThrAspSerAlaAspValHisLeuLysAspAlaA 1321

  3878 NTCTNTCAGACGGCATCGGAGGCAAAATCCGCCGCCGCGTGCTGCAT... 3924
       ::   :::      |||:::|||:::         |||:::|||:::
  1321 laGlyGluHisGlnIleAsnGlyArgLysAspGlyArgMetLeuTyrGly 1337

  3925 TACGGCATTCAGGCACGATAC.....................      3945
          |||::::::||||||:::
  1338 ValGlyLeuAsnAlaArgPheGlyAspAsnThrArgLeuGlyLeuGluVa 1354

  3946 ....CGCGCCGGTTTCGGCGGATTCGGCATCGAACCGTACATCGGCGCAA 3991
           |||::::::|||||   ::::::   :::      |||:::|||:
  1354 lGluArgSerAlaPheGlyLysTyrAsnThrAspAspAlaIleAsnAlaA 1371

  3992 CG...CGCTAT 3999
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  1371 snIleArgTyr 1374
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seq_documentation_block:

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ID   AAW27705 standard; Protein; 323 AA.
XX
AC   AAW27705;
XX
DT   08-MAY-1998  (first entry)
XX
DE   H. influenzae Hap protein autotransporter membrane integration region.
XX
KW   Hap protein; autotransporter; Gram-negative bacteria; diagnostic;
KW   therapy; surface presented polypeptide.
XX
OS   Haemophilus influenzae.
XX
PN   WO9735022-A1.
XX
PD   25-SEP-1997.
XX
PF   15-MAR-1996;   96WO-EP01130.
XX
PR   15-MAR-1996;   96WO-EP01130.
XX
PA   (PLAC ) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN.
XX
PI   Jose J,  Maurer J,  Meyer TF;
XX
DR   WPI; 1997-480227/44.
DR   N-PSDB; AAT88142.
XX
PT   Presentation of peptide(s) on surface of Gram-negative bacteria -
PT   via transformation with vector encoding signal peptide, presented
PT   peptide and transporter domain of auto-transporter, producing
PT   peptide libraries for epitope mapping
XX
PS   Claim 8; Fig 9; 84pp; German.
XX
CC   This sequence represents the H. influenzae Hap autotransporter membrane
CC   integration region. This region is involved in a novel method which
CC   allows the presentation of stable fusion polypeptides on the surface of
CC   Gram-negative bacteria which can be released into the surrounding media.
CC   The method can be used to produce a variegated population of
CC   surface-presented polypeptides, so that bacteria expressing polypeptides
CC   with particular properties can be identified and simultaneously selected,
CC   e.g. for epitope mapping or selection of ligands with the highest
CC   affinity for antibodies, major histocompatibility complex (MHC) molecules
CC   or other components of the immune system. Selected polypeptides can be
CC   used diagnostically, e.g. to screen sera or antibody banks, and
CC   polypeptide expressing cells may be used as live vaccines. They may also
CC   be used therapeutically, e.g. when the polypeptide is an antibody, to
CC   remove or concentrate pollutants, inactivate toxins, prepare and process
CC   food, prepare washing compositions and label cells. Selected bacteria can
CC   be stored, reproduced and replicated on a large scale as individual
CC   clones.
XX
SQ   Sequence   323 AA;
```

alignment_scores:

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            Quality:  709.50          Length:    311
              Ratio:  2.920             Gaps:      3
 Percent Similarity:  78.135   Percent Identity: 44.051
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alignment_block:

US-09-303-518D-651 x AAW27705 ..

Align seg 1/1 to: AAW27705 from: 1 to: 323

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  3439 GATTTGCCGCAA.....................CCGCAGCCCCAACCGCA 3467
       |||   ||||||                     |||   :::   ::
    14 AspAlaProGlnGlnSerGluLysAspArgLeuAlaGlnGluGluAlaGl 30

  3468 ACCTCAACCCCAACCGCAGCGCGACCTGATNAGCCGTTATGCCAATAGCG 3517
       :   |||   :::   |||:::||||||   |||||||||:::|||||||:
    30 uLysGln...ArgLysGlnLysAspLeuIleSerArgTyrSerAsnSerA 46

  3518 GTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTTTTCGCCGTACAGGAC 3567
       ::|||||||||:::|||||||||:::||||||::::::::::|||||||||
    46 laLeuSerGluLeuSerAlaThrValAsnSerMetLeuSerValGlnAsp 62

  3568 GAATTGGACCGCGTGTTTGCCGAAGACCGCCGCAACGCNGTTTGGACAAG 3617
       ||||||||||||:::|||:::::::::   ::::::||||||||||||::
    63 GluLeuAspArgLeuPheValAspGlnAlaGlnSerAlaValTrpThrAs 79

  3618 CNGCATCCGGNACACCAAACACTACCGTTCGCAAGATTTCCGCGCCTACC 3667
       :      :::      :::::::|||   |||:::   ||||||||||||:
    79 nIleAlaGlnAspLysArgArgTyrAspSerAspAlaPheArgAlaTyrG 96

  3668 GCCAACAA...ACCGACCTGCGCCAAATCGGTATGCAGAAAAACCTCGGC 3714
       ::||||||   |||:::|||||||||||||||:::||||||   |||:::
    96 lnGlnGlnLysThrAsnLeuArgGlnIleGlyValGlnLysAlaLeuAla 112

  3715 AGCGGGCGCGTCGGCATCCTGTTTTCGCACAACCGGACCGAAAACANCTT 3764
       :::|||||||:::|||   :::|||||||||:::|||:::::::|||:::||
   113 AsnGlyArgIleGlyAlaValPheSerHisSerArgSerAspAsnThrPh 129
```

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 3765 CGACGACGGCATCGGCAACTCGGCACGGCTTGCCCACGGCGCCGTTTTCG 3814
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  129 eAspGluGlnValLysAsnHisAlaThrLeuThrMetMetSerGlyPheA 146

 3815 GGCAATACGGCATCGGCAGGTTCGACATCGGCATCAGCACGGGCGCGGGT 3864
      ::||||||     |||  :::::::::|||:::::::::|||:::|||
  146 laGlnTyrGlnTrpGlyAspLeuGlnPheGlyValAsnValGlyThrGly 162

 3865 TTTAGCAGCGGCANTCTNTCAGACGGCATCGGAGGCAAAATCCGCCGCCG 3914
      :::|||:::::  :::::::::     :::  ||||||:::|||::
  163 IleSerAlaSerLysMetAlaGluGluGlnSerArgLysIleHisArgLy 179

 3915 CGTGCTGCATTACGGCATTCAGGCACGATACCGCGCCGGTTTCGGCGGAT 3964
      ::::::::::||||||::::::|||   |||:::     :::|||  :
  179 sAlaIleAsnTyrGlyValAsnAlaSerTyrGlnPheArgLeuGlyGlnL 196

 3965 TCGGCATCGAACCGTACATCGGCGCAACGCGCTATTTCGTCCAAAAAGCG 4014
      ::||||||:::||||||:::|||:::::::||||||||::::::::
  196 euGlyIleGlnProTyrPheGlyValAsnArgTyrPheIleGluArgGlu 212

 4015 GATTACCGCTACGAAAACGTCAATATCGCCACCCCCGGTCTTGCGTTCAA 4064
      :::|||:::   |||:::|||:::::   ||||||:::|||||||||
  213 AsnTyrGlnSerGluGluValArgValLysThrProSerLeuAlaPheAs 229

 4065 CCGNTACCGNGCGGGCATTAAGGCAGATTATTCATTCAAACCGGCGCAAC 4114
      |||||||:::|||||||||:::::::|||||:::|||   |||:::::::
  229 nArgTyrAsnAlaGlyIleArgValAspTyrThrPheThrProThrAspA 246

 4115 ACATNTCCATCACNCCTTATTTNAGCCTGTCCTATACCGATGCCGCTTCG 4164
      ::   |||:::   ||||||      ::::::|||:::|||:::::::::
  246 snIleSerValLysProTyrPhePheValAsnTyrValAspValSerAsn 262

 4165 GGCAAAGTCCGAACACGCGTCAATACCGCNGTATTGGCTCAGGATTTCGG 4214
      ::::::|||:::|||   ||||||   :::|||||   |||   |||||
  263 AlaAsnValGlnThrThrValAsnLeuThrValLeuGlnGlnProPheGl 279

 4215 CAAAACCCGCAGTGCGGAATGGGGCGTAAACGCCGAAATCAAAGGTTTCA 4264
      |:::      :::   |||   |||::::::|||||||||      |||
  279 yArgTyrTrpGlnLysGluValGlyLeuLysAlaGluIleLeuHisPheG 296

 4265 CGCTGTCCNTCCACGCTGCCGCCGCCAAAGGNCCGCAACTGGAAGCGCAA 4314
        :::|||:::      :::   ::::::|||   ||||||      |||
  296 lnIleSerAlaPheIleSerLysSerGlnGlySerGlnLeuGlyLysGln 312

 4315 CACAGCGCGGGCATCAAATTAGGCTACCGCTGG 4347
      :::::::::|||:::|||||||||||||||||
  313 GlnAsnValGlyValLysLeuGlyTyrArgTrp 323

seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1988.DAT:AAP80136

seq_documentation_block:
ID   AAP80136 standard; protein;  741 AA.
XX
AC   AAP80136;
XX
DT   09-OCT-1990  (first entry)
XX
DE   Neisseria IgA-Protease precursor protein.
XX
KW   IgA-Protease precursor; Neisseria sp;
KW   Gram-negative bacterial live vaccines.
XX
OS   Neisseria gonorrhoeae (strain SMH).
XX
FH   Key             Location/Qualifiers
FT   Cleavage-site   193..197
FT                   /label=IgA-Protease cleavage site (a)
FT   Cleavage-site   226..229
FT                   /label=IgA-Protease cleavage site (b)
FT   Cleavage-site   327..332
FT                   /label=IgA-Protease cleavage site (c)
XX
PN   DE3622221-A.
XX
PD   14-JAN-1988.
XX
PF   02-JUL-1986;   86DE-3622221.
XX
PR   02-JUL-1986;   86DE-3622221.
XX
PA   (PLAC ) MAX PLANCK GES WISSENSCH.
XX
PI   Meyer TF,  Halter R,  Pohlner J;
XX
DR   WPI; 1988-015104/03.
DR   N-PSDB; AAN80154.
XX
PT   Extracellular prodn. of proteins -
PT   by gram-negative host cells contg. a vector contg. one or more
PT   genes coding the desired protein
XX
PS   Disclosure; ; ; German.
XX
CC   Precursor protein consists of three regions i.e. Amino terminal
CC   leader sequence, IgA protease and a "helper" domain. The cleavage
CC   sites given in the features lie in the region between the latter
CC   two domains. DNA encoding a desired protein can be cloned into the
CC   corresponding region in the IgA protease precursor gene, between
CC   the DNA that encodes the natural cleavage sites. Thus, IgA protease
CC   coding region is not disrupted and the desired protein is released
CC   following cleavage by the protease.
XX
SQ   Sequence   741 AA;


alignment_scores:
            Quality:  385.50              Length:    785
              Ratio:  1.083                 Gaps:     18
 Percent Similarity:  45.350   Percent Identity: 20.892

alignment_block:
 US-09-303-518D-651 x AAP80136   ..

 Align seq 1/1  to: AAP80136  from: 1  to: 741

 2500 CTTTCCGACAACGCTAAGGCAAACGTAAGCCATTCCGCACTCAACGGCAA 2549
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    1 LeuSerAspLysAlaLeuAsnSerPheAspAlaThrProIleAsnGlyAs 17

 2550 TGTCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAACAGCCGCTTTA 2599
      ||||:::|||   :::::::|||::::::   :::   ::::::   :::
   17 nValAsnLeuAsnGlnAsnAlaAlaLeuValLeuGlyLysAlaAlaLeuT 34

 2600 CCGGACAACTCAGCGGCAGCAAGGANACAGCATTACACTTA...AAAGAC 2646
        |||::::::::::|||:::      :::   :::   |||   :::
   34 rpGlyLysIleGlnGlyGlnGlyAsnSerArgValSerLeuAsnGlnHis 50

 2647 AGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTGA 2696
      |||:::|||   |||   :::   :::::::::   ||||||:::|||
   51 SerLysTrpHisLeuThrGlyAspSerGlnValHisAsnLeuSerLeuAl 67

 2697 CAACGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCTGCAGGCG 2746
       ::::::   |||   ||||||:::|||          ||||||   :::|
   67 aAspSerHisIleHisLeuAsnAsnAla......SerAspAlaGlnSerA 82

 2747 CGCAAACCGGCAGNGTGTCAGACACGCCGCGCCGCCGTTCGCGCCGTTCC 2796
      ||
   82 la..................................................  82

 2797 CTATTATCCGTTACACCGCCAACTTCGGTAGAATCCCGTTTCAACACGCT 2846
                                          :::::::::::|||::
   83 ..............................AsnLysTyrHisThrIl 88

 2847 GACGGTAAACGGCAAATTGAACNGTCAAGGAACATTCCGCTTTATGTCGG 2896
      :   :::|||      |||:::   :::|||   |||:::::::::::
   88 eLysIleAsn...HisLeuSerGlyAsnGlyHisPheHisTyrLeuThrA 104
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2897 AACTCTTCGGCTACCGAAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAA 2946
      ::|||              :::|||||:::   :::   ||||||:::::
 104 spLeuAlaLysAsnLeuGlyAspLysValLeuValLysGluSerAlaSer 120

2947 GGNACTTACACCTTGGCGGTCAACAATACCGGCAACGAACCC......GT 2990
     |||   |||   |||   |||:::|||     :::||||||
 121 GlyHisTyrGlnLeuHisValGlnAsnLysThrGlyGluProAsnGlnGl 137

2991 AAGCCTCGATCAATTGACGGTAGTGGAAGGGAAAGACAACAAACCGCTGT 3040
       :::||||||   :::   :::   :::   :::|||:::
 137 uGlyLeuAspLeuPheAspAlaSerSerValGlnAspArg.......... 150

3041 CCGAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGATGCCGGCGCG 3090
       ::::::|||     :::|||   |||:::::::||||||   ||||||
 151 ..SerArgLeuPheValSerLeuAlaAsnHisTyrValAspLeuGlyAla 166

3091 TGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGCATAAT.. 3138
        ||||||   :::      :::::::|||     ||||||:::|||
 167 LeuArgTyrThrIleLysThrGluAsnGlyIleThrArgLeuTyrAsnPr 183

3139 ..................CCGGTCAAAGAACAAGAGCTTTCCGACAAAC 3169
                       |||||||||
 183 oTyrAlaGlyAsnGlyArgProValLysProAlaProSerProAlaAlaA 200

3170 TCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCG...... 3213
           ::::::|||:::|||   ::::::   |||:::|||
 200 snThrAlaSerGlnAlaGlnLysAlaThrGlnThrAspGlyAlaGlnIle 216

3214 ..............................................CA 3215
                                                   ||
 217 AlaLysProGlnAsnIleValValAlaProProSerProGlnAlaAsnGl 233

3216 AAGCCTTGACGCGCTGATTGCGGCCGGGCGCGATGCCGCCGAAAAGACAG 3265
     |:::   :::||||||       ::::::         |||   :
 233 nAlaGluGluAlaLeuArgGlnGlnAlaLysAlaGluGlnValLysArgG 250

3266 AAAGCGTTGCCGAACCGGCCCGGCNGGCAGGCGGGGAAAATGTCGGCATT 3315
     ::::::::||||||     :::   |||
 250 lnGlnAlaAlaGluAlaGluLysValAla..................... 259

3316 ATGCAGGCGGAGGAAGAGAAAAAACGGGTGCAGGCGGAT........... 3354
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 260 ArgGlnLysAspGluGluAlaLysArgLysAlaAlaGluIleAlaArgGl 276

3354 .................................................. 3354

 276 nGlnGluGluAlaArgLysAlaAlaGluLeuAlaAlaLysGlnLysAlaG 293

3355 ..........AAAGACAGCGCNTTGGCGAAACAGCGCGAAGCGGAAACC 3393
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 293 luAlaGluArgLysAlaArgGluLeuAlaArgGlnLysAlaGluGluAla 309

3394 CGGCCGGNTACCACCGCCTTCCCCCGCGCCCGCNGCGCCCGCCGGGATTT 3443
              ::::::|||   |||:::   |||     |||     ||
 310 SerHisGlnAlaAsnAlaLysProLysArgArgArgArgArgAlaIleLe 326

3444 GCCGCAACCG....................................... 3453
     ||||:::|||
 326 uProArgProProAlaProValPheSerLeuAspAspTyrAspAlaLysA 343

3453 .................................................. 3453

 343 spAsnSerGluSerSerIleGlyAsnLeuAlaArgValIleProArgMet 359

3453 .................................................. 3453

 360 GlyArgGluLeuIleAsnAspTyrGluGluIleProLeuGluGluLeuGl 376

3453 .................................................. 3453

 376 uAspGluAlaGluGluGluArgArgGlnAlaThrGlnPheHisSerLysS 393

3453 .................................................. 3453

 393 erArgAsnArgArgAlaIleSerSerGluProSerSerAspGluAspAla 409

3453 .................................................. 3453

 410 SerGluSerValSerThrSerAspLysHisProGlnAspAsnThrGluLe 426

3454 ..........................CAGCCC.........CAACCGC 3466
                               ||||||          ||||||:
 426 uHisGluLysValGluThrAlaGlyLeuGlnProArgAlaAlaGlnProA 443

3467 AACCTCAACCCCAACCGCAGCGCGACCTGATNAGCCGTTATGCCAATAGC 3516
      ::   |||            |||   |||      |||      :::||||||
 443 rgThrGlnAlaAlaAlaGlnAlaAspAlaValSerThrAsnThrAsnSer 459

3517 GGTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTT.............. 3552
     :::||||||:::         |||:::   :::|||:::
 460 AlaLeuSerAspAlaMetAlaSerThrGlnSerIleLeuLeuAspThrGl 476

3553 ....TTCGCCGTACAGGACGAATTGGACCGCGTGTTTGCCGAAGACCGCC 3598
        :::   ::::::         ::::::      |||:::   ::::
 476 yAlaTyrLeuThrArgHisIleAlaGlnLysSerArgAlaAspAlaGluL 493

3599 GCAACGCNGTTTGGACAAGCNGCATCCGGNACACCAAACACTACCGTTCG 3648
     :::|||:::||||||   |||               :::   |||   |||
 493 ysAsnSerValTrpMetSerAsnThrGlyTyrGlyArgAspTyrAlaSer 509

3649 CAAGATTTCCGCGCCTACCGCCAACAAACCGACCTGCGCCAAATCGGTAT 3698
        ::::::|||   :::   ::::::                |||||||||::
 510 AlaGlnTyrArgArgPheSerSerLysArgThrGlnThrGlnIleGlyIl 526

3699 GCAGAAAAACCTCGGCAGCGGG...CGCGTCGGCATCCTGTTTTCGCACA 3745
     ::::::::::|||::::::::     ::::::|||   ::::::::::::
 526 eAspArgSerLeuSerGluAsnMetGlnIleGlyGlyValLeuThrTyrS 543

3746 ACCGGACCGAAAACANCTTCGACGACGGCATCGGCAACTCGGCACGGCTT 3795
     ::   ::::::::::::||||||::::::   |||::::::      :::
 543 erAspSerGlnHisThrPheAspGlnAla...GlyGlyLysAsnThrPhe 558

3796 GCCCACGGCGCCGTTTTCGGGCAATACGGCATCGGC...AGGTTCGACAT 3842
     :::::::::   ::::::|||:::|||   ::::::      :::   ::
 559 ValGlnAlaAsnLeuTyrGlyLysTyrTyrLeuAsnAspAlaTrpTyrVa 575

3843 CGGCATCAGCACGGGCGCGGGTTTAGCAGCGGCANTCTNTCAGACGGCA 3892
     ::::   :::      |||||||||        :::   |||:::
 575 lAlaGlyAspIleGlyAlaGlySerLeuArgSerArgLeuGlnThrGlnG 592

3893 TCGGAGGCAAAATCCGCCGCCGCGTGCTGCATTACGGCATTCAGGCACGA 3942
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 592 lnLysAlaAsnPheAsnArgThrSerIleGlnThrGlyLeuThrLeuGly 608

3943 TACCGCGCCGGTTTCGGCGGATTCGGCATCGAACCGTACATCGGCGCAAC 3992
               ::::::   |||   |||   |||      |||
 609 AsnThrLeuLysIleAsnGlnPheGluIleValProSerAlaGlyIleAr 625

3993 GCGCTATTTCGTCCAAAAAGCGGATTACCGCTACGAAAACGTCAATATCG 4042
               :::::::::|||||||||:::      :::   ::::::
 625 gTyrSerArgLeuSerSerAlaAspTyrLysLeuGlyAspAspSerValL 642

4043 CCACCCCCGGTCTTGCGTTCAACCGNTACCGNGCGGGCATTAAGGCAGAT 4092
        :::   ::::::|||   :::            ||||||:::
 642 ysValSerSerMetAlaValLysThrLeuThrAlaGlyLeuAspPheAla 658

4093 TATTCATTCAAACCGGCGCAACACATNTCCATCACNCCTTATTTNAGCCT 4142
     |||   ||||||   :::   :::   ::::::   |||      |||
 659 TyrArgPheLys...ValGlyAsnLeuThrValLysProLeuLeuSerAl 674

4143 GTCCTATACCGATGCCGCTTCGGGCAAAGTCCGAACACGCGTCAATACCG 4192
        :::|||      |||      ||||||      ::::::|||:::
 674 aAlaTyrPhe...AlaAsnTyrGlyLysGlyGlyValAsnValGlyGlyL 690

4193 CNGTATTGGCTCAGGATTTCGGCAAAACCCGCAGTGCGGAATGGGGCGTA 4242
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 690 ysSerPheAlaTyrLysAlaAspAsnGlnGlnGlnTyrSerAlaGlyVal 706

4243 AACGCCGAAATCAAAGGTTTCACGCTGTCCNTCCACGCTGCCGCCGCCAA 4292
              ::::::   |||||||:::   :::::::::   :::||
 707 AlaLeuLeuTyrArgAsnValThrLeuAsnValAsnGlySerIleThrLy 723

4293 AGGNCCGCAACTGGAAGCGCAACACAGCGCGGGCATCAAATTAGGCTACC 4342
     ||||   |||||||||   |||   |||:::   |||||||:::     |
 723 sGlyLysGlnLeuGluLysGlnLysSerGlyGlnIleLysIleGlnIleA 740

4343 GCTGG 4347
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 740 rgPhe 741

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seq_documentation_block:
ID   AAG98842 standard; Protein; 1569 AA.
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AC   AAG98842;
XX
DT   26-SEP-2001  (first entry)
XX
DE   E. coli growth and proliferation related protein sequence SEQ ID NO:312.
XX
KW   Escherichia coli; growth; proliferation; microbial; antimicrobial;
KW   bacterial infection; microorganism.
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OS   Escherichia coli.
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PN   WO200134810-A2.
XX
PD   17-MAY-2001.
XX
PF   09-NOV-2000; 2000WO-US30950.
XX
PR   09-NOV-1999;   99US-0164415.
XX
PA   (ELIT-) ELITRA PHARM INC.
XX
PI   Forsyth RA,  Ohlsen K,  Zyskind J;
XX
DR   WPI; 2001-335933/35.
DR   N-PSDB; AAH84513.
XX
PT   Novel nucleic acids that inhibit Escherichia coli proliferation, useful
PT   for screening for homologous genes and for designing expression vectors
PT   -
XX
PS   Claim 19; Page 396-399; 522pp; English.
XX
CC   AAH84373 to AAH84499 represent Escherichia coli growth and proliferation
CC   related DNA sequences (I). AAH84500 to AAH84670 encode the E. coli
CC   growth and proliferation related proteins given in AAG99078 and AAG98830
CC   to AAG98999. (I) can be used as potential targets for the generation of
CC   new antimicrobial agents, and for identification of compounds which
CC   interact with the gene products of (I). In addition the expression of
CC   (I) and the purification of the proteins, the purified proteins can be
CC   used to generate reagents and screen small molecule libraries or other
CC   candidate compound libraries for compounds that can be further developed
CC   to yield novel antimicrobial compounds. In addition, nucleic acid probes
CC   complementary to (I) that are specific for particular species of
CC   microorganisms can be used to identify particular microorganism species
CC   in clinical specimens, therefore, providing a rapid and dependable
CC   method by which to identify the causative agents of a bacterial
CC   infection. Also, antibodies generated against proteins translated from
CC   mRNA transcribed from proliferation-required sequences can also be used
CC   to screen for specific microorganisms that produce such proteins in a
CC   species-specific manner. AAH84371 and AAH84670 represent sequencing
CC   primers used in the isolation of E. coli growth and proliferation
CC   related sequence, which are used in an example from the present
CC   invention.
XX
SQ   Sequence   1569 AA;

alignment_scores:
            Quality:  372.50              Length:   1676
              Ratio:  0.491                 Gaps:     76
 Percent Similarity:  45.286   Percent Identity: 19.153

alignment_block:
 US-09-303-518D-651 x AAG98842   ..

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  160 GlyThrThrIleGluSerGlyAsnGlnAspValTyrLysGlyGlyIleSe 176

  177 AAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTNTACAACA 226
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  176 rAsnGlyThrThrIleLysGlyGlyAlaSerArgValGluGlyGlySerA 193

  227 AAAAAGGGGAGTTGGTC......GGCAAATCAATGACAAAAGCCCCG... 267
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  193 laAsnGlyIleLeuIleAspGlyGlySerGlnIleValLysValGlnGly 209

  268 ATGATTGATTTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTG.. 315
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  316 ..............................GGCGATCAATATATT. 330
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  331 ................GTGAGCGTGGCACATAACGGCGGCTATAACAAC 363
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  243 luGlnSerThrValGluThrThrThrIleLysAsnGlyGlyGluGlnArg 259

  364 GTT.................GATTTTGGTGCGGAAGGAAGNAATCCCGA 395
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  260 ValTyrGluSerArgAlaLeuAspThrThrIleGluGlyGlyThrGlnSe 276

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  276 rLeuAsnSerLysSer.........................ThrAlaL 284

  446 ACAATTCACACCCTTACAACGGCGATTANCATATGCCGCGTTTGCATAAA 495
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  284 ysAsnThrHisIleTyrSerGlyGlyThr.........GlnIleValAsp 297

  496 TTTGTCACAGATGCAGAACCTGTCGAAATGACGAGT............GA 533
      ::::::   ::::::   :::|||:::   |||             ||
  298 AsnThrSerThrSerAspValIleGluValTyrSerGlyGlyValLeuAs 314

  534 CATGAGGGGGAATACCTATTCCGATAAAGAAAAATATCCCGAGCGTGTCC 583
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  314 pValArgGlyGlyThrAlaThrAsnValThrGln.............. 325

  584 GCATCGGCTCAGGACACCACTATTGGCGTTATGATGATGACAAACACGGC 633

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  634 GATTTATCCTACTCCGGCGCATGGTTAATTGGCGGCAATACACAT..... 678
            ::::::||||||   ::::::      |||||||::
  326 .........HisAspGlyAla...IleLeuLysThrAsnThrAsnGlyTh 338

  679 ....ATGCAGGGTTGGGGAAATAATGGCGTANTTAGTTTG.......... 714
      ::::::|||   :::::::::|||:::   |||:::
  338 rThrValSerGlyThrAsnSerGluGlyAlaPheSerIleHisAsnHisV 355

  715 ......................AGCGGCGATGTGCGCCATGCCAACGAC 741
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  355 alAlaAspAsnValLeuLeuGluAsnGlyGlyHisLeuAspIleAsnAla 371
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 942 TTTTGAACCGCGCAGTAACGGACATTTTTCCTTTACATCCAACAACAACG 991
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1042 ......AAAGTACAGACAGTCCGACTGTTTGACGAATCTTTGAATGAAAC 1085
           |||::::::|||:::   :::   :::   |||   :::   ::
 444 GlyGlyLysAlaAspThrThrIleIleSerSerGlySerArgGlnValVa 460

1086 TGATAAAGAACCAGTT..............TACGCGGCAGGGGGTGTTA 1120
     :::::|||:::   :::                  :::|||||||||
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 476 ....................................SerLeuIleVal 479

1171 TACGGCAACGGCAAACTCATCTTATCAAACAACATCAACCAAGGCGCGGG 1220
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 493 ySerAlaLeuValAlaAsn.............................. 499

1271 CGTGGCAAGGCGCGGGCGTTCATATCAGT..............GAAGAC 1305
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1356 AATCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGGGAAAACCAAGGCT 1405
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 524 .......................TyrValValLeuGluAsnThrGlyG 532

1406 CGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCAGGCAGACGAT 1455
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1456 AAAGGCAAA............AAACAAGCCTTTAGTGAAATCGGCTTGNT 1493
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 549 GlyGlyLysLeuIleValGlnLysGluAlaLysThrAsp........... 561

1494 CAGCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCG 1543
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1544 ACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCAT 1593
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 567 ..................AsnGlyGlyValLeuGluValGlnAspGly 576

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1726 AGACTTAATTACAGCAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAA 1775
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1776 AGATACGACCAAAACGAACGGGCGGCTCAACCTT.............. 1809
              ::::::|||||||:::::::::::::
 638 pThrIleIleAsnAlaAsnGlyLysMetAspValTyrGlyLysAspValG 655

1810 ..............................GTTTACCAGCCCGCCGCA 1827
                                    :::|||      |||:::
 655 lyThrValLeuAsnSerAlaGlyThrGlnThrIleTyrAlaSerAlaThr 671

1828 GAAGACCGCACCCNGCTGCTTTCCGGCGGAACAAATTTAAACGGCAACAT 1877
     :::|||:::::::   :::   :::|||       ::::::   |||
 672 SerAspLysAlaAsnIleLysGlyGlyLysGlnThrValTyrGlyLeuAl 688

1878 CACGCAAACAAAC.........GGCAAACTGTTTTTCAGCGGCAGACCGA 1918
      |||:::::::|||          |||:::   :::   :::|||      |
 688 aThrGluAlaAsnIleGluSerGlyGluGlnIleValAspGlyGlySerT 705

1919 CACCGCACGCCTACAATCATTTAGGAAGCGGGTGGTCAAAAATGGAAGGT 1968
     ||             :::|||::::::::::|||   :::   :::::::::
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1969 ATCCCACAAGGA.........GAAATCGTGTGGGACAACGACTGGATCNA 2009
           ::::::         :::||||||         :::   |||
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2010 CCGCACGTTTAAAGCGGAAAATTTCCATATTCAGGGCGGGCAGGCGGTGA 2059
        :::      ||||||:::      |||:::||||||:::   |||:
 736 tAlaAsnGlyThrAlaGluGlySerIleIleAsnGlyGlySerGlnValV 753

2060 TTTCCCGC..................................... 2067
     ::::::::
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2068 ...AATGTTGCCAAAGTGGAAGGCGATTGNCATTTGAGCAATCACGCCCA 2114
        ::|||   :::      :::   :::   :::::::::   :::||
 770 LeuAspValArgGluLysGlySerAlaThrGlyIleGlnGlnSerSerGl 786

2115 AGCAGTTTTTGGTGTCGCACCGCATCAAAGCCATACAATCTGTACACGTT 2164
     |:::::::::   ::::::   :::   :::::::::      ||||||:
 786 nGlyAlaLeuValAlaThrThrArgAlaThrArgValThrGlyThrArgA 803

2165 CGGACTGGACN.................GGTCTGACAAAT......... 2187
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 820 LeuAlaAsnGlyGlyValLeuThrValGluSerAspThrSerSerAspLy 836

2217 AGTGATTGCTTCATTG.....................ACTAAGACNGACN 2245
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2246 TNAGCGGCANTGTNAGNCTNNCCNATNACGNTNNTTNAAANCTCNCNGGG 2295
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2296 CNTGCNNCACTNAANGGC.............................. 2313
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862 GluGlnIleValGluGlyValAlaAsnGluThrThrIleAsnAspGlyGl 878
2314 .....AATCTTAGTGCAAATGGCGAT.....ACACGTTATACAG 2347
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2348 TCAGCCACAACGCCACCCAAAACGGCAAC.....CTTAGCCTCGTG 2388
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2439 GGNTTCGGGCAAT.....GCTTCATTTAATCTAAGCAACAACGCCG 2479
927 uIleSerGlyThrHisGlnTyrGlyThrPheSerIleSerGlyAsnLeuA 944
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961 ThrGluAlaArgAspSerThrValGlyLysGlyGly..... 972
2562 CGATAAGGCAGTATTCCATTTTGAAAACAGCCGCTTTACCGGACAACTCA 2611
973 .....AlaMetGlnAsnLeuGlyGlnAspSerAlaThrLysValAsnS 987
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987 erGlyGlyGlnTyrThrLeuGlyArgSerLysAspGluPheGlnAlaLeu 1003
2662 CCGTCAGGCACGGAATTA..... 2679
1004 AlaArgAlaGluAspLeuGlnValAlaGlyGlyThrAlaIleValTyrAl 1020
2680 .....GGCAATTTAAACC 2692
1020 aGlyThrLeuAlaAspAlaSerValSerGlyAlaThrGlySerLeuSerL 1037
2693 TT..... 2694
1037 euMetThrProArgAspAsnValThrProValLysLeuGluGlyAlaVal 1053
2695 .....GACAACGCCACCATTACACTCAATTCCGCCTAT..... 2727
1054 ArgIleThrAspSerAlaThrLeuThrLeuGlyAsnGlyValAspThrTh 1070
2728 .CGCCACGATGCTGCAGGCGCGCAAACCGGCAGNGTG..... 2763
1070 rLeuAlaAspLeuThrAlaAlaSerArgGlySerValTrpLeuAsnSerA 1087
2764 .....TCAGACACGCCGCGCCGCCGTTCGCGC...CGTTCCCTA 2799
1087 snAsnSerCysAlaGlyThrSerAsnCysGluTyrArgValAsnSerLeu 1103
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1104 LeuLeuAsnAspGlyAspValTyrLeuSerAlaGlnThrAlaAlaProAl 1120
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1120 aThrThrAsnGlyIleTyrAsnThrLeuThrThrAsn...GluLeuSerG 1136
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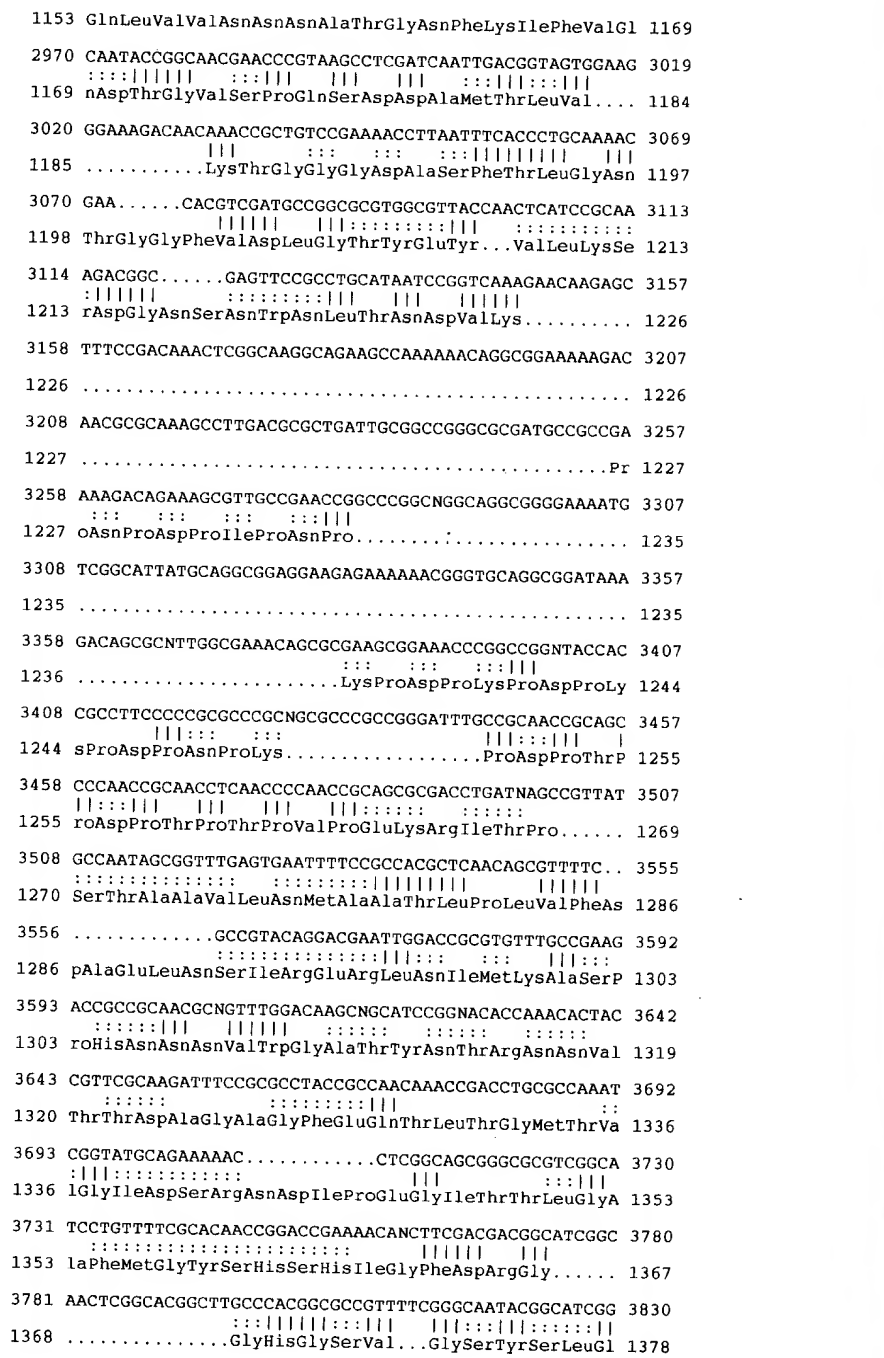
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3114 AGACGGC.....GAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGC 3157
1213 rAspGlyAsnSerAsnTrpAsnLeuThrAsnAspValLys..... 1226
3158 TTTCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGAC 3207
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3308 TCGGCATTATGCAGGCGGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAA 3357
1235 1235
3358 GACAGCGCNTTGGCGAAACAGCGCGAAGCGGAAACCCGGCCGGNTACCAC 3407
1236 .....LysProAspProLysProAspProLy 1244
3408 CGCCTTCCCCCGCGCCCGCNGCGCCCGCCGGGATTTGCCGCAACCGCAGC 3457
1244 sProAspProAsnProLys.....ProAspProThrP 1255
3458 CCCAACCGCAACCTCAACCCCAACCGCAGCGCGACCTGATNAGCCGTTAT 3507
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3508 GCCAATAGCGGTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTTTTC.. 3555
1270 SerThrAlaAlaValLeuAsnMetAlaAlaThrLeuProLeuValPheAs 1286
3556 .....GCCGTACAGGACGAATTGGACCGCGTGTTTGCCGAAG 3592
1286 pAlaGluLeuAsnSerIleArgGluArgLeuAsnIleMetLysAlaSerP 1303
3593 ACCGCCGCAACGCNGTTTGGACAAGCNGCATCCGGNACACCAAACACTAC 3642
1303 roHisAsnAsnAsnValTrpGlyAlaThrTyrAsnThrArgAsnAsnVal 1319
3643 CGTTCGCAAGATTTCCGCGCCTACCGCCAACAAACCGACCTGCGCCAAAT 3692
1320 ThrThrAspAlaGlyAlaGlyPheGluGlnThrLeuThrGlyMetThrVa 1336
3693 CGGTATGCAGAAAAAC.....CTCGGCAGCGGGCGCGTCGGCA 3730
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3731 TCCTGTTTTCGCACAACCGGACCGAAAACANCTTCGACGACGGCATCGGC 3780
1353 laPheMetGlyTyrSerHisSerHisIleGlyPheAspArgGly..... 1367
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1368 .....GlyHisGlySerVal...GlySerTyrSerLeuGl 1378

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  3831 C.............................................. 3831
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  1378 yGlyTyrAlaSerTrpGluHisGluSerGlyPheTyrLeuAspGlyValV 1395

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  1395 alLysLeuAsnArgPheLysSerAsnValAlaGlyLysMetSerSerGly 1411

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       ::::::   :::::::::      |||:::|||:::||||||
  1412 GlyAlaAlaAsnGlySerTyrHisSerAsnGlyLeuGlyGlyHis..... 1426

  3909 CCGCCGCGTGCTGCATTACGGCATTCAGGCACGATACCGCGCCGGTTTCG 3958
                            |||::::::      |||         |
  1427 .....................IleGluThrGlyMetArgPheThrAspG 1436

  3959 GCGGATTCGGCATCGAACCGTACATCGGCGCAACGCGCTATTTCGTCCAA 4008
       ||::::::::::::   ||||||   :::   |||   :::   ::::::
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  4009 AAAGCGGATTACCGCTACGAAAAC............GTCAATATCGCCAC 4046
       :::   :::|||:::   :::|||                ::::::   ||
  1453 AsnProGluTyrHisLeuSerAsnGlyMetLysSerLysSerValAspTh 1469

  4047 CCCCGGTCTTGCGTTCAACCGNTACCGN...GCGGGCATTAAGGCAGATT 4093
       |   ::::::           ||||||      |||          :::|
  1469 rArgSerIle............TyrArgGluLeuGlyAlaThrLeuSerT 1482

  4094 ATTCATTCAAACCGGCGCAACACATNTCCATCACNCCTTATTTNAGCCTG 4143
       ||:::::::::   ::::::      ::::::   |||:::   :::
  1482 yrAsnMetArgLeuGlyAsnGlyMetGluValGluProTrpLeuLysAla 1498

  4144 TCCTATACCGATGCCGCTTCGGGCAAAGTCCGAACACGCGTCAATACCGC 4193
       :::                        |||::::::||||||:::
  1499 AlaValArgLysGluPheValAspAspAsnArgValLysValAsnSerAs 1515

  4194 NGTATTGGCTCAGGATTTC......GGCAAAACCCGCAGTGCGGAATGGG 4237
                       ::::::      |||:::          :::   |
  1515 pGlyAsnPheValAsnTyrLeuSerGlyArgArgGlyIleTyrGlnAlaG 1532

  4238 GCGTAAACGCCGAAATCAAAGGTTTCACGCTGTCCNTCCACGCTGCCGCC 4287
       ||::::::|||:::::::::::::   |||||||||   |||   ::::::
  1532 lyIleLysAlaSerPheSerSer...ThrLeuSerGlyHisLeuGlyVal 1547

  4288 GCCAAAGGNCCGCAACTGGAAGCGCAACACAGCGCGGGCATCAAA..... 4332
       :::                       :::||||||||||||:::::
  1548 Gly.................TyrSerHisSerAlaGlyValGluSerPr 1558

  4333 .............TTAGGCTACCGCTGG 4347
                    |||   :::|||
  1558 oTrpAsnAlaValAlaGlyValAsnTrp 1567
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seq_documentation_block:
ID   AAR63505 standard; Protein; 1536 AA.
XX
AC   AAR63505;
XX
DT   25-JUN-1995  (first entry)
XX
DE   Haemophilus high molecular weight protein HMW1.
XX
KW   High molecular weight protein; HMW1; protective vaccine; otitis;
KW   sinusitis; bronchitis; Hib.
XX
OS   Haemophilus.
XX
PN   WO9421290-A.
XX
PD   29-SEP-1994.
XX
PF   15-MAR-1994;   94WO-US02550.
XX
PR   16-MAR-1993;   93US-0038682.
XX
PA   (BARE/) BARENKAMP S J.
PA   (SGEM/) ST GEME J W.
XX
PI   Barenkamp SJ,  St GEME JW;
XX
DR   WPI; 1994-316665/39.
DR   Q-PSDB; Q72293.
XX
PT   New immunogenic high mol. wt. proteins of non typeable
PT   Haemophilus - useful in protective vaccines
XX
PS    Claim 2; Page 31; 127pp; English.
XX
CC   The HMW1 protein encoded by this sequence is useful in a vaccine to
CC   protect against disease caused by non-typeable Haemophilus which are
CC   not controlled by H. influenzae type b (Hib) vaccines.  The encoded
CC   protein can also be used as a carrier for protective Hib
CC   polysaccharide (in a conjugate vaccin against meningitis) or for
CC   other antigens, haptens, etc.
XX
SQ   Sequence   1536 AA;
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              Ratio:  0.482                 Gaps:     58
 Percent Similarity:  49.872   Percent Identity: 20.460

alignment_block:
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     349 GlyGluThrTyrLeuGly.........................GlyAs 356

     177 AAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTNTACAACA 226
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     356 pGluArgGlyGlu.........GlyLysLysGlyIleGlnLeuAlaLysL 370

     227 AAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGAT 276
         ||                    |||:::   |||:::      |||:::
     370 ys..................ThrSerLeuGluLysGlySerThrIleAsn 380

     277 TTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAATA 326
           |||       ::::::::::|||   |||   :::   ||||||
     381 ValSerGlyLysGluLysGlyGlyArgAlaIleValTrpGlyAspIleAl 397

     327 TATTGTG................................AGCGTGGCACATA 346
          ::::::                              :::::|||   :
     397 aLeuIleAspGlyAsnIleAsnAlaGlnGlySerGlyAspIleAlaLysT 414

     347 ACGGCGGCTAT................................AACAAC 363
         ::|||||:::                                 :::|||
     414 hrGlyGlyPheValGluThrSerGlyHisAspLeuPheIleLysAspAsn 430

     364 ......GTTGATTTTGGTGCGGAAGGAAGNAATCCCGATCAGCACCGTTT 407
               ||||||                :::|||||:::      ::
     431 AlaIleValAspAlaLysGluTrpLeuLeuAspProAspAsnValSerIl 447

     408 TTCTTACCAAATTGTGAAAAGAAATAATTATAAGCCTGACAATTCACACC 457
         ::::   :::   :::   |||:::|||   :::   |||::::::::::
     447 eAsnAlaGluThrAlaGlyArgSerAsnThrSerGluAspAspGluTyrT 464

     458 CTTACAACGGCGAT...TANCATATGCCGCGTTTGCATAAATTTGTCACA 504
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     464 hrGlySerGlyAsnSerAlaSerThrProLysArgAsnLysGluLysThr 480
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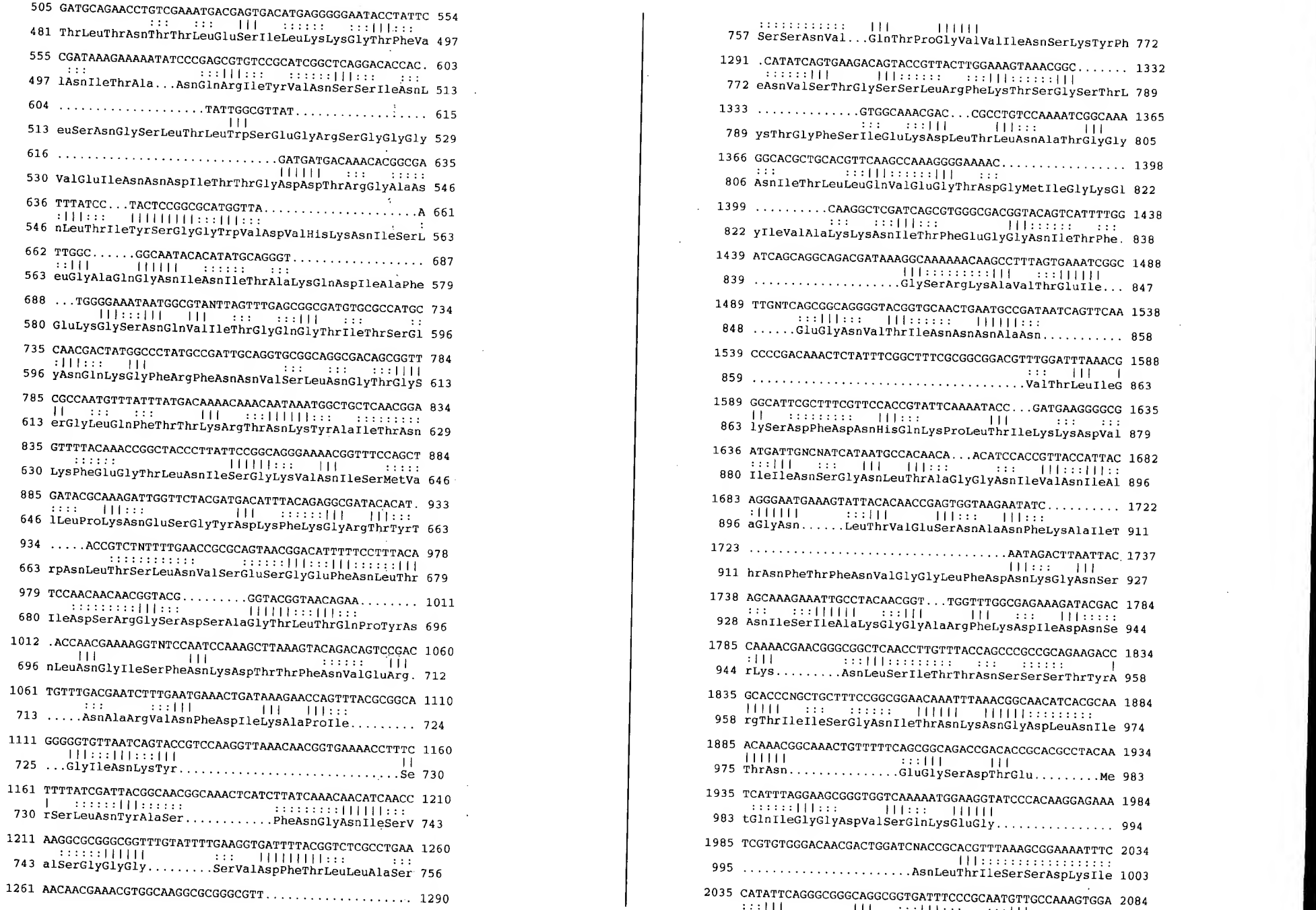

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1019 nSerAspSerAspAlaThrAsnAsnAlaAsnLeu..............  1030

2135 CGCATCAAAGCCATACAATCTGTACACGTTCGGACTGGACNGGTCTGACA 2184
                 ||||||   |||:::
1031 .............ThrIleLysThrLys.....................  1035

2185 AATTGTGTCGAANAAANCATTACCGACGATAAAGTGATTGCTTCATTGAC 2234
           |||      :::|||:::|||     |||:::::::::::
1036 .........GluLeuLysLeuThrGlnAspLeuAsnIleSerGlyPheAs 1049

2235 TAAGACNGACNTNAGCGGCANTGTNAGNCTNNCCNATNACGNTNNTTNAA 2284
     :|||::::::   ::::::
1049 nLysAlaGluIleThrAlaLys............................  1056

2285 ANCTCNCNGGGCNTGCNNCACTNAANGGCAATCTT...AGTGCAAATGGC 2331
          |||:::            ||||||     |||||||:::|||
1057 .....AspGlySerAspLeuThrIleGlyAsnThrAsnSerAlaAspGly 1071

2332 GATACACGTTATACAGTCAGCCACAACGCCACCCAAAACGGCAACCTTAG 2381
       :::         |||:::   |||   ::::::::::::::::||
1072 ThrAsnAlaLysLysValThrPheAsnGlnValLysAspSerLysIleSe 1088

2382 CCTCGTGGGCAATGCCCAAGCAACATTTAATCAAGCCACATTAAACGGCA 2431
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1088 rAlaAspGly.................HisLysValThrLeuHisSerL 1099

2432 ACNCATCGGNTTCGGGCAATGCTTCATTTAATCTAAGCAACAACGCCGCA 2481
     ::   ::::::|||||||:::   :::   |||   ::::::::::::
1099 ysValGluThrSerGlySerAsnAsn...AsnThrGluAspSerSerAsp 1114

2482 CAAAACGGCAGTCTGACGCTTTCCGACAACGCTAAGGCAAACGTAAGCCA 2531
     :::|||:::::::|||||||:::      :::||||||   |||||||:::
1115 AsnAsnAlaGlyLeuThrIle......AspAlaLys...AsnValThr.. 1127

2532 TTCCGCACTCAACGGCAATGTCTCCCTAGCCGATAAGGCAGTATTCCATT 2581
           :::|||:::|||::::::   :::   |||||||||
1128 .......ValAsnAsnAsnIleThr...SerHisLysAlaVal....... 1138

2582 TTGAAAACAGCCGCTTTACCGGACAACTCAGCGGCAGCAAGGANACAGCA 2631
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2632 TTACACTTAAAA......GACAGCGAATGGACGCTGCCGTCAGGCACGGA 2675
     ::::::            :::   |||   |||      :::|||:::
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2676 ATTAGGCAATTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCT 2725
      ||||||:::::::::   ::::::::::::::::||||||:::::::::
1171 eLeuGlyGlyIleGluSerSerSerGlySerValThrLeuThrAlaThr. 1187

2726 ATCGCCACGATGCTGCAGGCGCGCAAACCGGCAGNGTGTCAGACACGCCG 2775
           ::::::|||   |||   ::::::      :::::::|||
1188 ........GluGlyAlaLeuAlaValSerAsnIleSerGlyAsnThrVal 1201

2776 CGCCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGT 2825
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2826 AGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACNGTCAAG 2875
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1218 eLysGlyThrGluSerValThrThrSerSerGlnSerGlyAspIleGlyG 1235

2876 GAACATTC.....................CGCTTTATGTCGGAACTCTTC 2904
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1235 lyThrIleSerGlyGlyThrValGluValLysAlaThrGluSerLeuThr 1251

2905 GGCTACCGAAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGNACTTA 2954
           ::::::|||::::|||   |||   ::::::|||::::::
1252 ThrGlnSerAsnSerLysIleLys...AlaThrThrGlyGluAlaAsnVa 1267

2955 CACCTTGGCGGTC.....................AACAATACCGGCA 2980
      |||   |||:::                     :::|||||   |
1267 lThrSerAlaThrGlyThrIleGlyGlyThrIleSerGlyAsnThrValA 1284

2981 ACGAACCCGTAAGCCTCGATCAATTGACGGTA.................. 3012
     ||      ::::::     :::|||||||||
1284 snValThrAlaAsnAlaGlyAspLeuThrValGlyAsnGlyAlaGluIle 1300

3013 ......GTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTT 3056
           :::||||||     :::        |||:::::::
1301 AsnAlaThrGluGlyAlaAlaThrLeuThrThrSerSerGlyLysLeuTh 1317

3057 CACCCTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACTCA 3106
       |||      :::::::|||:::   ::: |||:::|||   :::|||
1317 rThrGluAlaSerSerHisIleThrSer.AlaLysGlyGlnValAsnLeu 1333

3107 TCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAG 3156
     |||||||:::   :::|||   |||      |||::::::   |||   ::
1334 SerAlaGlnAspGlySerValAlaGlySerIleAsnAlaAlaAsnValTh 1350

3157 CTTTCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGA 3206
     ::::   |||:::::::::            |||:::   :::   ::::
1350 rLeuAsnThrThrGlyThrLeuThrThrValLysGlySerAsnIleAsnA 1367

3207 CAACGCGCAAAGCCTTG 3223
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1367 laThrSerGlyThrLeu 1372
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seq_documentation_block:

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ID   AAB01846 standard; Protein; 1536 AA.
XX
AC   AAB01846;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain 12 HMW1A protein, SEQ ID NO:67.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain 12.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52195.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Example 16; Fig 28A-Q; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
```

CC promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC and the hmwB and hmwC genes encode accessory proteins which are
CC responsible for post-translational processing and secretion of the HMWA
CC proteins. The modified hmwABC operon used in the expression construct of
CC the invention contains an A gene modified such that it encodes only the
CC mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC vectors are used for the production of recombinant H. influenzae HMW
CC proteins which can be used as vaccines to mediate a humoral or
CC cell-mediated immune response to provide protection against diseases in
CC humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC antigens in immunoassays for detecting antibodies against Haemophilus,
CC HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC HMW proteins can be used to isolate and clone hmw genes from other
CC non-typeable strains of Haemophilus via hybridisation reactions. The
CC present sequence represents an HMWA protein from a non-typeable strain of
CC H. influenzae.
XX
SQ Sequence 1536 AA;

alignment_scores:
Quality: 282.00 Length: 1173
Ratio: 0.482 Gaps: 58
Percent Similarity: 49.872 Percent Identity: 20.460

alignment_block:
US-09-303-518D-651 x AAB01846 ..

Align seg 1/1 to: AAB01846 from: 1 to: 1536

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 349 GlyGluThrTyrLeuGly.........................GlyAs 356

 177 AAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTNTACAACA 226
     :::::::|||:::         |||   |||   |||::::::   :::|
 356 pGluArgGlyGlu.........GlyLysLysGlyIleGlnLeuAlaLysL 370

 227 AAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGAT 276
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 277 TTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAATA 326
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 381 ValSerGlyLysGluLysGlyGlyArgAlaIleValTrpGlyAspIleAl 397

 327 TATTGTG............................AGCGTGGCACATA 346
      ::::::                           ::::::|||   :
 397 aLeuIleAspGlyAsnIleAsnAlaGlnGlySerGlyAspIleAlaLysT 414

 347 ACGGCGGCTAT..............................AACAAC 363
     ::|||||||:::                             :::|||
 414 hrGlyGlyPheValGluThrSerGlyHisAspLeuPheIleLysAspAsn 430

 364 ......GTTGATTTTGGTGCGGAAGGAAGNAATCCCGATCAGCACCGTTT 407
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 431 AlaIleValAspAlaLysGluTrpLeuLeuAspProAspAsnValSerIl 447

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     ::::   :::   :::   |||:::|||   :::   |||:::::::::
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 458 CTTACAACGGCGAT...TANCATATGCCGCGTTTGCATAAATTTGTCACA 504
         :::|||:::   :::      |||:::   :::|||      |||
 464 hrGlySerGlyAsnSerAlaSerThrProLysArgAsnLysGluLysThr 480

 505 GATGCAGAACCTGTCGAAATGACGAGTGACATGAGGGGGAATACCTATTC 554
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 481 ThrLeuThrAsnThrThrLeuGluSerIleLeuLysLysGlyThrPheVa 497

 555 CGATAAAGAAAAATATCCCGAGCGTGTCCGCATCGGCTCAGGACACCAC. 603
      :::                 :::|||:::   ::::::|||:::   :::
 497 lAsnIleThrAla...AsnGlnArgIleTyrValAsnSerSerIleAsnL 513

 604 ...................TATTGGCGTTAT..................... 615
                              |||
 513 euSerAsnGlySerLeuThrLeuTrpSerGluGlyArgSerGlyGlyGly 529

 616 ............................GATGATGACAAACACGGCGA 635
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 530 ValGluIleAsnAsnAspIleThrThrGlyAspAspThrArgGlyAlaAs 546

 636 TTTATCC...TACTCCGGCGCATGGTTA.....................A 661
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 546 nLeuThrIleTyrSerGlyGlyTrpValAspValHisLysAsnIleSerL 563

 662 TTGGC......GGCAATACACATATGCAGGGT..................... 687
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           |||:::|||   |||   :::   :::|||   :::      ::
 580 GluLysGlySerAsnGlnValIleThrGlyGlnGlyThrIleThrSerGl 596

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 613 erGlyLeuGlnPheThrThrLysArgThrAsnLysTyrAlaIleThrAsn 629

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 630 LysPheGluGlyThrLeuAsnIleSerGlyLysValAsnIleSerMetVa 646

 885 GATACGCAAAGATTGGTTCTACGATGACATTTACAGAGGCGATACACAT. 933
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 646 lLeuProLysAsnGluSerGlyTyrAspLysPheLysGlyArgThrTyrT 663

 934 .....ACCGTCTNTTTTGAACCGCGCAGTAACGGACATTTTTCCTTTACA 978
           ::::::::::::      ::::::|||:::|||::::::|||
 663 rpAsnLeuThrSerLeuAsnValSerGluSerGlyGluPheAsnLeuThr 679

 979 TCCAACAACAACGGTACG.........GGTACGGTAACAGAA........ 1011
       :::::::::|||:::          ||||||:::|||:::
 680 IleAspSerArgGlySerAspSerAlaGlyThrLeuThrGlnProTyrAs 696

1012 .ACCAACGAAAAGGTNTCCAATCCAAAGCTTAAAGTACAGACAGTCCGAC 1060
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 696 nLeuAsnGlyIleSerPheAsnLysAspThrThrPheAsnValGluArg. 712

1061 TGTTTGACGAATCTTTGAATGAAACTGATAAAGAACCAGTTTACGCGGCA 1110
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1111 GGGGGTGTTAATCAGTACCGTCCAAGGTTAAACAACGGTGAAAACCTTTC 1160
       |||:::|||:::|||                              ||
 725 ...GlyIleAsnLysTyr.............................Se 730

1161 TTTTATCGATTACGGCAACGGCAAACTCATCTTATCAAACAACATCAACC 1210
     |   ::::::|||:::::::          :::::::::||||||:::
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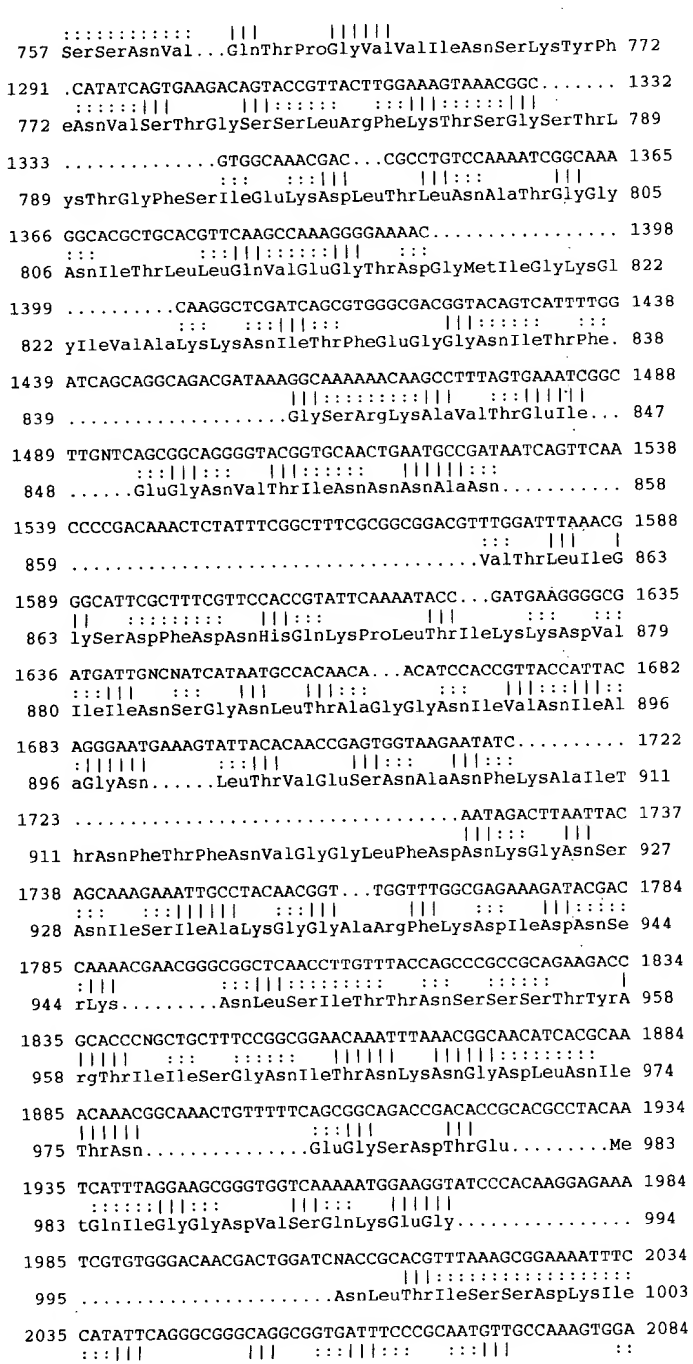
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.....ValThrLeuIleG 863
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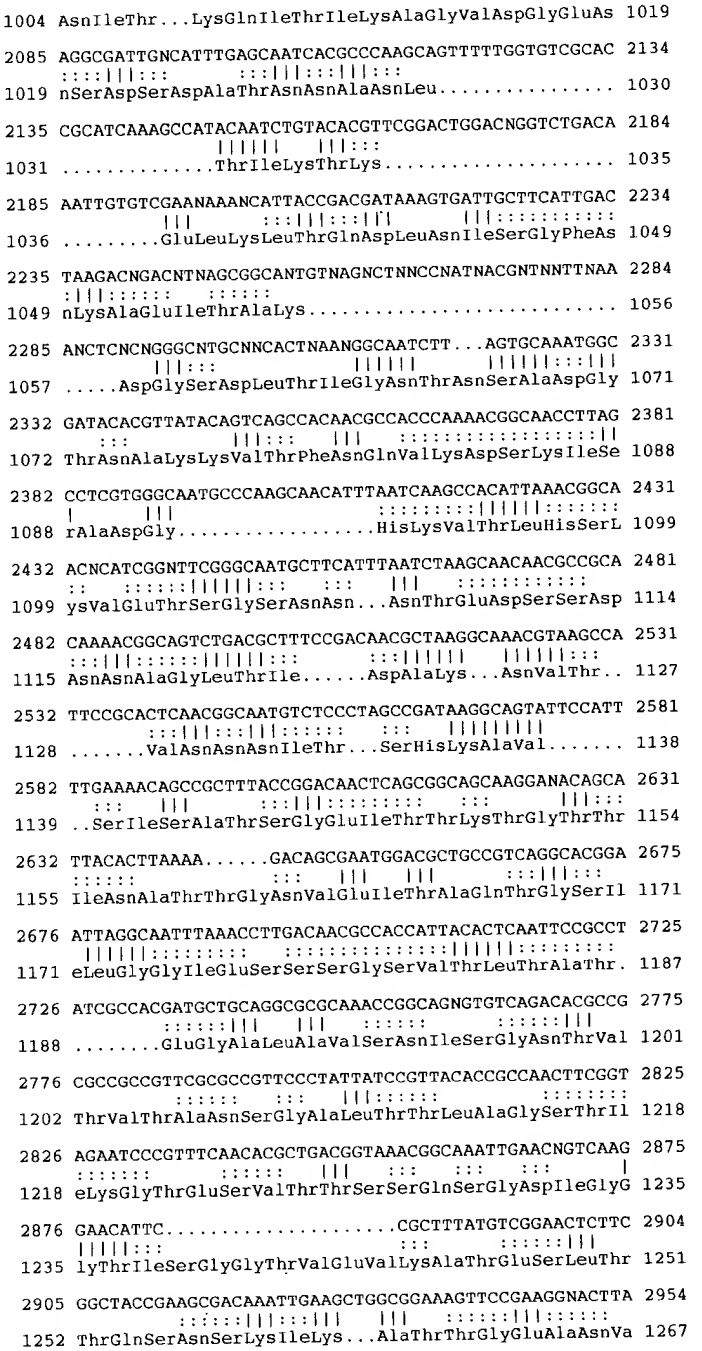
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.....ThrIleLysThrLys..... 1035
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.....GluLeuLysLeuThrGlnAspLeuAsnIleSerGlyPheAs 1049
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.....AspGlySerAspLeuThrIleGlyAsnThrAsnSerAlaAspGly 1071
GATACACGTTATACAGTCAGCCACAACGCCACCCAAAACGGCAACCTTAG 2381
ThrAsnAlaLysLysValThrPheAsnGlnValLysAspSerLysIleSe 1088
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rAlaAspGly.....HisLysValThrLeuHisSerL 1099
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ysValGluThrSerGlySerAsnAsn...AsnThrGluAspSerSerAsp 1114
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AsnAsnAlaGlyLeuThrIle.....AspAlaLys...AsnValThr.. 1127
TTCCGCACTCAACGGCAATGTCTCCCTAGCCGATAAGGCAGTATTCCATT 2581
.....ValAsnAsnAsnIleThr...SerHisLysAlaVal..... 1138
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ThrGlnSerAsnSerLysIleLys...AlaThrThrGlyGluAlaAsnVa 1267

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2955 CACCTTGGCGGTC.....................AACAATACCGGCA 2980
1267 lThrSerAlaThrGlyThrIleGlyGlyThrIleSerGlyAsnThrValA 1284

2981 ACGAACCCGTAAGCCTCGATCAATTGACGGTA..................  3012
1284 snValThrAlaAsnAlaGlyAspLeuThrValGlyAsnGlyAlaGluIle 1300

3013 ......GTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTT 3056
1301 AsnAlaThrGluGlyAlaAlaThrLeuThrThrSerSerGlyLysLeuTh 1317

3057 CACCCTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACTCA 3106
1317 rThrGluAlaSerSerHisIleThrSer.AlaLysGlyGlnValAsnLeu 1333

3107 TCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAG 3156
1334 SerAlaGlnAspGlySerValAlaGlySerIleAsnAlaAlaAsnValTh 1350

3157 CTTTCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGA 3206
1350 rLeuAsnThrThrGlyThrLeuThrThrValLysGlySerAsnIleAsnA 1367

3207 CAACGCGCAAAGCCTTG 3223
1367 laThrSerGlyThrLeu 1372
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1997.DAT:AAW30293

seq_documentation_block:

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ID   AAW30293 standard; Protein; 1536 AA.
XX
AC   AAW30293;
XX
DT   14-APR-1998  (first entry)
XX
DE   Non-typeable Haemophilus high mol.wt. surface protein HMW1.
XX
KW   Non-typeable Haemophilus; high molecular weight surface protein;
KW   HMW1; hmw1A gene; immunogen; vaccine; otitis media.
XX
OS   Haemophilus influenzae strain 12.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 4
FT                   /note= "encoded by CTA"
FT   Misc-difference 98
FT                   /note= "encoded by GAT"
FT   Misc-difference 363
FT                   /note= "encoded by AAG"
XX
PN   WO9736914-A1.
XX
PD   09-OCT-1997.
XX
PF   01-APR-1997;   97WO-US04707.
XX
PR   01-APR-1996;   96US-0617697.
XX
PA   (BARE/) BARENKAMP S J.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1997-503038/46.
DR   N-PSDB; AAT90994 and AAT90996.
XX
PT   High molecular weight proteins of non-typeable Haemophilus
PT   influenzae - useful for vaccine production
XX
PS   Claim 7; Page 66-70; 183pp; English.
XX
CC   This protein comprises the high molecular weight surface protein
CC   HMW1 (125 kDa) of non-typeable Haemophilus influenzae strain 12 that
CC   has the immunological ability to protect against disease caused by a
CC   non-typeable Haemophilus strain and is characterised by at least
CC   one surface-exposed B-cell epitope that is recognised by monoclonal
CC   antibody AD6.  The HMW1 amino acid sequence was deduced from the
CC   hmw1 gene sequence (see AAT90994 and AAT90996).  The expressed protein
CC   is truncated, starting at residue 442 of the full-length gene
CC   product.  HMW2 (see AAW30294), HMW3 (see AAW30291) and HMW4 (see
CC   AAW30292) have also been identified.  A conjugate comprising HMW1
CC   linked to an antigen, hapten or polysaccharide, and a synthetic
CC   peptide of 6-150 amino acids corresponding to at least protective
CC   epitope of HMW1 are also claimed.  HMW proteins, conjugates and
CC   peptides can be used in vaccines, as immunogens for preparation of
CC   antibodies and as antigens for detection of these antibodies.
XX
SQ   Sequence   1536 AA;
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alignment_scores:

Quality:	277.00	Length:	1173
Ratio:	0.474	Gaps:	58
Percent Similarity:	49.872	Percent Identity:	20.375

alignment_block:

US-09-303-518D-651 x AAW30293 ..

Align seg 1/1 to: AAW30293 from: 1 to: 1536

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349 GlyGluThrTyrLeuGly.........................GlyAs 356

177 AAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTNTACAACA 226
356 pGluArgGlyGlu.........GlyLysAsnGlyIleGlnLeuAlaLysL 370

227 AAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGAT 276
370 ys..................ThrSerLeuGluLysGlySerThrIleAsn 380

277 TTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAATA 326
381 ValSerGlyLysGluLysGlyGlyArgAlaIleValTrpGlyAspIleAl 397

327 TATTGTG.............................AGCGTGGCACATA 346
397 aLeuIleAspGlyAsnIleAsnAlaGlnGlySerGlyAspIleAlaLysT 414

347 ACGGCGGCTAT...............................AACAAC 363
414 hrGlyGlyPheValGluThrSerGlyHisAspLeuPheIleLysAspAsn 430

364 ......GTTGATTTTGGTGCGGAAGGAAGNAATCCCGATCAGCACCGTTT 407
431 AlaIleValAspAlaLysGluTrpLeuLeuAspProAspAsnValSerIl 447

408 TTCTTACCAAATTGTGAAAAGAAATAATTATAAGCCTGACAATTCACACC 457
447 eAsnAlaGluThrAlaGlyArgSerAsnThrSerGluAspAspGluTyrT 464

458 CTTACAACGGCGAT...TANCATATGCCGCGTTTGCATAAATTTGTCACA 504
464 hrGlySerGlyAsnSerAlaSerThrProLysArgAsnLysGluLysThr 480

505 GATGCAGAACCTGTCGAAATGACGAGTGACATGAGGGGGAATACCTATTC 554
481 ThrLeuThrAsnThrThrLeuGluSerIleLeuLysLysGlyThrPheVa 497

555 CGATAAAGAAAAATATCCCGAGCGTGTCCGCATCGGCTCAGGACACCAC. 603
497 lAsnIleThrAla...AsnGlnArgIleTyrValAsnSerSerIleAsnL 513
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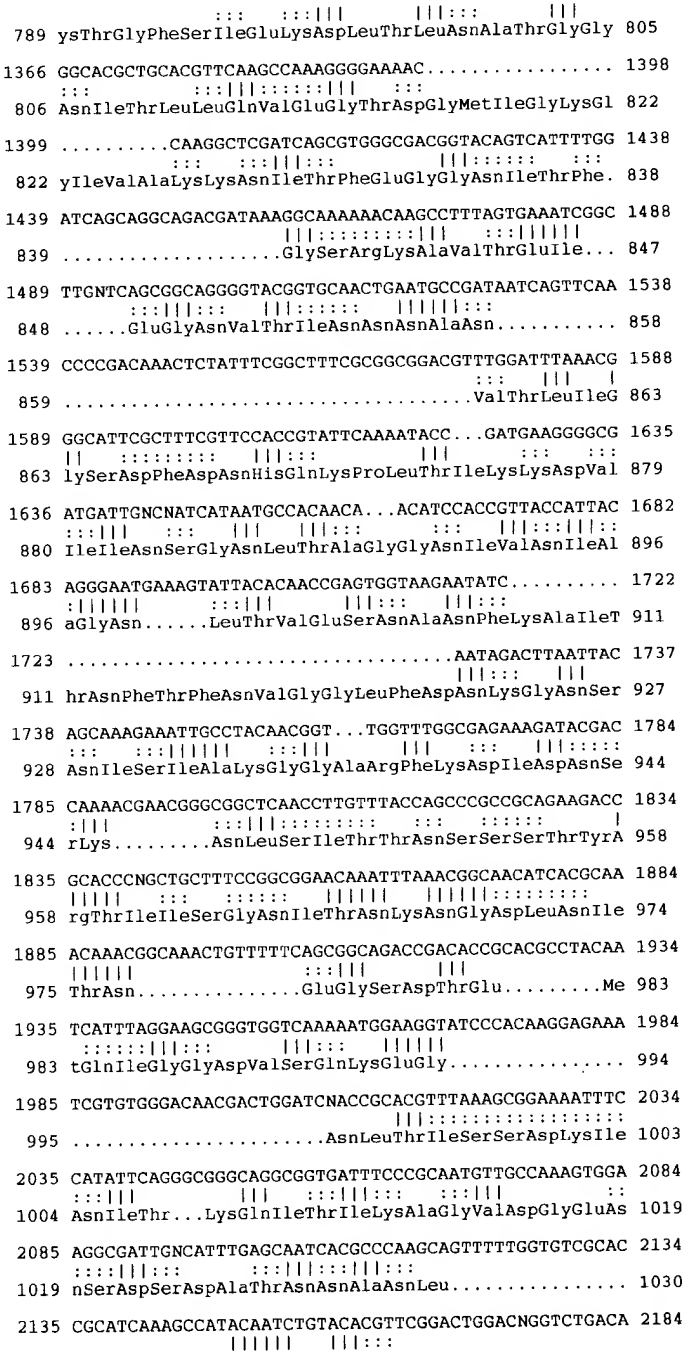
604 ..TATTGGCGTTAT.. 615
513 euSerAsnGlySerLeuThrLeuTrpSerGluGlyArgSerGlyGlyGly 529
616 ..GATGATGACAAACACGGCGA 635
530 ValGluIleAsnAsnAspIleThrThrGlyAspAspThrArgGlyAlaAs 546
636 TTTATCC...TACTCCGGCGCATGGTTA....A 661
546 nLeuThrIleTyrSerGlyGlyTrpValAspValHisLysAsnIleSerL 563
662 TTGGC......GGCAATACACATATGCAGGGT.. 687
563 euGlyAlaGlnGlyAsnIleAsnIleThrAlaLysGlnAspIleAlaPhe 579
688 ...TGGGGAAATAATGGCGTANTTAGTTTGAGCGGCGATGTGCGCCATGC 734
580 GluLysGlySerAsnGlnValIleThrGlyGlnGlyThrIleThrSerGl 596
735 CAACGACTATGGCCCTATGCCGATTGCAGGTGCGGCAGGCGACAGCGGTT 784
596 yAsnGlnLysGlyPheArgPheAsnAsnValSerLeuAsnGlyThrGlyS 613
785 CGCCAATGTTTATTTATGACAAAACAAACAATAAATGGCTGCTCAACGGA 834
613 erGlyLeuGlnPheThrThrLysArgThrAsnLysTyrAlaIleThrAsn 629
835 GTTTTACAAACCGGCTACCCTTATTCCGGCAGGGAAAACGGTTTCCAGCT 884
630 LysPheGluGlyThrLeuAsnIleSerGlyLysValAsnIleSerMetVa 646
885 GATACGCAAAGATTGGTTCTACGATGACATTTACAGAGGCGATACACAT. 933
646 lLeuProLysAsnGluSerGlyTyrAspLysPheLysGlyArgThrTyrT 663
934 .....ACCGTCTNTTTTGAACCGCGCAGTAACGGACATTTTTCCTTTACA 978
663 rpAsnLeuThrSerLeuAsnValSerGluSerGlyGluPheAsnLeuThr 679
979 TCCAACAACAACGGTACG.....GGTACGGTAACAGAA..... 1011
680 IleAspSerArgGlySerAspSerAlaGlyThrLeuThrGlnProTyrAs 696
1012 .ACCAACGAAAAGGTNTCCAATCCAAAGCTTAAAGTACAGACAGTCCGAC 1060
696 nLeuAsnGlyIleSerPheAsnLysAspThrThrPheAsnValGluArg. 712
1061 TGTTTGACGAATCTTTGAATGAAACTGATAAAGAACCAGTTTACGCGGCA 1110
713 .....AsnAlaArgValAsnPheAspIleLysAlaProIle..... 724
1111 GGGGGTGTTAATCAGTACCGTCCAAGGTTAAACAACGGTGAAAACCTTTC 1160
725 ...GlyIleAsnLysTyr.....Se 730
1161 TTTTATCGATTACGGCAACGGCAAACTCATCTTATCAAACAACATCAACC 1210
730 rSerLeuAsnTyrAlaSer.....PheAsnGlyAsnIleSerV 743
1211 AAGGCGCGGGCGGTTTGTATTTTGAAGGTGATTTTACGGTCTCGCCTGAA 1260
743 alSerGlyGlyGly.....SerValAspPheThrLeuLeuAlaSer 756
1261 AACAACGAAACGTGGCAAGGCGCGGGCGTT..... 1290
757 SerSerAsnVal...GlnThrProGlyValValIleAsnSerLysTyrPh 772
1291 .CATATCAGTGAAGACAGTACCGTTACTTGGAAAGTAAACGGC..... 1332
772 eAsnValSerThrGlySerSerLeuArgPheLysThrSerGlySerThrL 789
1333 .....GTGGCAAACGAC...CGCCTGTCCAAAATCGGCAAA 1365


789 ysThrGlyPheSerIleGluLysAspLeuThrLeuAsnAlaThrGlyGly 805
1366 GGCACGCTGCACGTTCAAGCCAAAGGGGAAAAC..... 1398
806 AsnIleThrLeuLeuGlnValGluGlyThrAspGlyMetIleGlyLysGl 822
1399 .....CAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGG 1438
822 yIleValAlaLysLysAsnIleThrPheGluGlyGlyAsnIleThrPhe. 838
1439 ATCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGC 1488
839 .....GlySerArgLysAlaValThrGluIle... 847
1489 TTGNTCAGCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAA 1538
848 .....GluGlyAsnValThrIleAsnAsnAsnAlaAsn..... 858
1539 CCCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACG 1588
859 .....ValThrLeuIleG 863
1589 GGCATTCGCTTTCGTTCCACCGTATTCAAAATACC...GATGAAGGGGCG 1635
863 lySerAspPheAspAsnHisGlnLysProLeuThrIleLysLysAspVal 879
1636 ATGATTGNCNATCATAATGCCACAACA...ACATCCACCGTTACCATTAC 1682
880 IleIleAsnSerGlyAsnLeuThrAlaGlyGlyAsnIleValAsnIleAl 896
1683 AGGGAATGAAAGTATTACACAACCGAGTGGTAAGAATATC..... 1722
896 aGlyAsn.....LeuThrValGluSerAsnAlaAsnPheLysAlaIleT 911
1723 .....AATAGACTTAATTAC 1737
911 hrAsnPheThrPheAsnValGlyGlyLeuPheAspAsnLysGlyAsnSer 927
1738 AGCAAAGAAATTGCCTACAACGGT...TGGTTTGGCGAGAAAGATACGAC 1784
928 AsnIleSerIleAlaLysGlyGlyAlaArgPheLysAspIleAspAsnSe 944
1785 CAAAACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACC 1834
944 rLys.....AsnLeuSerIleThrThrAsnSerSerSerThrTyrA 958
1835 GCACCCNGCTGCTTTCCGGCGGAACAAATTTAAACGGCAACATCACGCAA 1884
958 rgThrIleIleSerGlyAsnIleThrAsnLysAsnGlyAspLeuAsnIle 974
1885 ACAAACGGCAAACTGTTTTTCAGCGGCAGACCGACACCGCACGCCTACAA 1934
975 ThrAsn.....GluGlySerAspThrGlu.....Me 983
1935 TCATTTAGGAAGCGGGTGGTCAAAAATGGAAGGTATCCCACAAGGAGAAA 1984
983 tGlnIleGlyGlyAspValSerGlnLysGluGly..... 994
1985 TCGTGTGGGACAACGACTGGATCNACCGCACGTTTAAAGCGGAAAATTTC 2034
995 .....AsnLeuThrIleSerSerAspLysIle 1003
2035 CATATTCAGGGCGGGCAGGCGGTGATTTCCCGCAATGTTGCCAAAGTGGA 2084
1004 AsnIleThr...LysGlnIleThrIleLysAlaGlyValAspGlyGluAs 1019
2085 AGGCGATTGNCATTTGAGCAATCACGCCCAAGCAGTTTTTGGTGTCGCAC 2134
1019 nSerAspSerAspAlaThrAsnAsnAlaAsnLeu..... 1030
2135 CGCATCAAAGCCATACAATCTGTACACGTTCGGACTGGACNGGTCTGACA 2184

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1031 .............ThrIleLysThrLys..................... 1035

2185 AATTGTGTCGAANAAANCATTACCGACGATAAAGTGATTGCTTCATTGAC 2234
1036 .........GluLeuLysLeuThrGlnAspLeuAsnIleSerGlyPheAs 1049

2235 TAAGACNGACNTNAGCGGCANTGTNAGNCTNNCCNATNACGNTNNTTNAA 2284
1049 nLysAlaGluIleThrAlaLys........................... 1056

2285 ANCTCNCNGGGCNTGCNNCACTNAANGGCAATCTT...AGTGCAAATGGC 2331
1057 .....AspGlySerAspLeuThrIleGlyAsnThrAsnSerAlaAspGly 1071

2332 GATACACGTTATACAGTCAGCCACAACGCCACCCAAAACGGCAACCTTAG 2381
1072 ThrAsnAlaLysLysValThrPheAsnGlnValLysAspSerLysIleSe 1088

2382 CCTCGTGGGCAATGCCCAAGCAACATTTAATCAAGCCACATTAAACGGCA 2431
1088 rAlaAspGly.................HisLysValThrLeuHisSerL 1099

2432 ACNCATCGGNTTCGGGCAATGCTTCATTTAATCTAAGCAACAACGCCGCA 2481
1099 ysValGluThrSerGlySerAsnAsn...AsnThrGluHisSerSerAsp 1114

2482 CAAAACGGCAGTCTGACGCTTTCCGACAACGCTAAGGCAAACGTAAGCCA 2531
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2532 TTCCGCACTCAACGGCAATGTCTCCCTAGCCGATAAGGCAGTATTCCATT 2581
1128 .......ValAsnAsnAsnIleThr...SerHisLysAlaVal....... 1138

2582 TTGAAAACAGCCGCTTTACCGGACAACTCAGCGGCAGCAAGGANACAGCA 2631
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2632 TTACACTTAAAA......GACAGCGAATGGACGCTGCCGTCAGGCACGGA 2675
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2676 ATTAGGCAATTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCT 2725
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2726 ATCGCCACGATGCTGCAGGCGCGCAAACCGGCAGNGTGTCAGACACGCCG 2775
1188 ........GluGlyAlaLeuAlaValSerAsnIleSerGlyAsnThrVal 1201

2776 CGCCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGT 2825
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2826 AGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACNGTCAAG 2875
1218 eLysGlyThrGluSerValThrThrSerSerGlnSerGlyAspIleGlyG 1235

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2905 GGCTACCGAAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGNACTTA 2954
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1284 snValThrAlaAsnAlaGlyAspLeuThrValGlyAsnGlyAlaGluIle 1300

3013 ......GTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTT 3056
1301 AsnAlaThrGluGlyAlaAlaThrLeuThrThrSerSerGlyLysLeuTh 1317

3057 CACCCTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACTCA 3106
1317 rThrGluAlaSerSerHisIleThrSer.AlaLysGlyGlnValAsnLeu 1333

3107 TCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAG 3156
1334 SerAlaGlnAspGlySerValAlaGlySerIleAsnAlaAlaAsnValTh 1350

3157 CTTTCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGA 3206
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1367 laThrSerGlyThrLeu 1372
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seq_documentation_block:

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ID   AAR41723 standard; Protein; 1536 AA.
XX
AC   AAR41723;
XX
DT   26-APR-1994  (first entry)
XX
DE   High molecular weight protein 1 (HMW1).
XX
KW   HMW; high molecular weight protein; virus; vaccine; influenza;
KW   epitope; immunity; haemophilus influenzae.
XX
OS   Haemophilus influenzae.
XX
PN   WO9319090-A.
XX
PD   30-SEP-1993.
XX
PF   16-MAR-1993;   93WO-US02166.
XX
PR   16-MAR-1992;   92GB-0005704.
XX
PA   (BARE/) BARENKAMP S J.
PA   (INRM ) INSERM INST NAT SANTE & RECH MEDICALE.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1993-320683/40.
DR   N-PSDB; AAQ49506.
XX
PT   High molecular weight surface proteins - of non-typeable
PT   haemophilus which exhibit immunogenic properties
XX
PS   Claim 3; Figure 2; 100pp; English.
XX
CC   The isolation and purification of the high molecular weight protein
CC   enables the identification of the major protective epitopes of the
CC   protein by conventional epitope mapping.  These epitopes can then be
CC   synthesised using standard techniques and incorporated into fully
CC   synthetic or recombinant vaccines.
XX
SQ   Sequence   1536 AA;
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alignment_scores:

Quality:	271.00	Length:	1185
Ratio:	0.465	Gaps:	58
Percent Similarity:	49.198	Percent Identity:	20.084

alignment_block:

US-09-303-518D-651 x AAR41723 ..

Align seg 1/1 to: AAR41723 from: 1 to: 1536

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349 GlyGluThrTyrLeuGly.........................GlyAs 356

177 AAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTNTACAACA 226
    :::::::|||:::          |||   :::   |||:::::::   :::|
356 pGluArgGlyGlu.........GlyLysAsnGlyIleGlnLeuAlaLysL 370

227 AAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGAT 276
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370 ys..................ThrSerLeuGluLysGlySerThrIleAsn 380

277 TTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAATA 326
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381 ValSerGlyLysGluLysGlyGlyArgAlaIleValTrpGlyAspIleAl 397

327 TATTGTG................................AGCGTGGCACATA 346
    ::::::                              ::::::|||   :
397 aLeuIleAspGlyAsnIleAsnAlaGlnGlySerGlyAspIleAlaLysT 414

347 ACGGCGGC.......................................... 354
    ::|||||||
414 hrGlyGlyPheValGluThrSerGlyHisAspLeuPheIleLysAspAsn 430

355 ..............................TATAACAACGTTGATTT 371
                                  ::::::||||||:::::
431 AlaIleValAspAlaLysGluTrpLeuLeuAspPheAspAsnValSerIl 447

372 TGGTGCGGAAGGAAGNAATCCCGATCAGCACCGTTTTTCTTACCAAATTG 421
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447 eAsnAlaGluThrAlaGly.............................. 453

422 TGAAAAGAAATAATTATAAGCCTGACAATTCACACCCTTACAACGGCGAT 471
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454 .....ArgSerAsnThrSerGluAspAspGluTyrThrGlySerGlyAsn 468

472 ...TANCATATGCCGCGTTTGCATAAATTTGTCACAGATGCAGAACCTGT 518
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469 SerAlaSerThrProLysArgAsnLysGluLysThrThrLeuThrAsnTh 485

519 CGAAATGACGAGTGACATGAGGGGGAATACCTATTCCGATAAAGAAAAAT 568
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485 rThrLeuGluSerIleLeuLysLysGlyThrPheValAsnIleThrAla. 501

569 ATCCCGAGCGTGTCCGCATCGGCTCAGGACACCAC.............. 603
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502 ..AsnGlnArgIleTyrValAsnSerSerIleAsnLeuSerAsnGlySer 517

604 ......TATTGGCGTTAT............................... 615
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518 LeuThrLeuTrpSerGluGlyArgSerGlyGlyGlyValGluIleAsnAs 534

616 ..............GATGATGACAAACACGGCGATTTATCC...TACT 646
                |||||||   :::   :::::::|||:::   ||||
534 nAspIleThrThrGlyAspAspThrArgGlyAlaAsnLeuThrIleTyrS 551

647 CCGGCGCATGGTTA.....................ATTGGC......GGC 669
    ||||||:::|||:::                    :::|||      |||
551 erGlyGlyTrpValAspValHisLysAsnIleSerLeuGlyAlaGlnGly 567

670 AATACACATATGCAGGGT.....................TGGGGAAATAA 698
    |||   ::::::   :::                          |||:::||
568 AsnIleAsnIleThrAlaLysGlnAspIleAlaPheGluLysGlySerAs 584

699 TGGCGTANTTAGTTTGAGCGGCGATGTGCGCCATGCCAACGACTATGGCC 748
    |   |||   :::   :::|||   :::      :::|||:::   |||
584 nGlnValIleThrGlyGlnGlyThrIleThrSerGlyAsnGlnLysGlyP 601

749 CTATGCCGATTGCAGGTGCGGCAGGCGACAGCGGTTCGCCAATGTTTATT 798
                                  :::   :::   :::|||||   :::   :::
601 heArgPheAsnAsnValSerLeuAsnGlyThrGlySerGlyLeuGlnPhe 617

799 TATGACAAAACAAACAATAAATGGCTGCTCAACGGAGTTTTACAAACCGG 848
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618 ThrThrLysArgThrAsnLysTyrAlaIleThrAsnLysPheGluGlyTh 634

849 CTACCCTTATTCCGGCAGGGAAAACGGTTTCCAGCTGATACGCAAAGATT 898
              ||||||:::   |||      :::::::::   |||:::
634 rLeuAsnIleSerGlyLysValAsnIleSerMetValLeuProLysAsnG 651

899 GGTTCTACGATGACATTTACAGAGGCGATACACAT......ACCGTCTNT 942
              |||   ::::::|||   |||:::         ::::::
651 luSerGlyTyrAspLysPheLysGlyArgThrTyrTrpAsnLeuThrSer 667

943 TTTGAACCGCGCAGTAACGGACATTTTTCCTTTACATCCAACAACAACGG 992
    ::::::      ::::::|||:::|||::::::|||   :::::::::||
668 LeuAsnValSerGluSerGlyGluPheAsnLeuThrIleAspSerArgGl 684

993 TACG.........GGTACGGTAACAGAA.........ACCAACGAAAAGG 1024
    |:::         ||||||:::|||:::             |||
684 ySerAspSerAlaGlyThrLeuThrGlnProTyrAsnLeuAsnGlyIleS 701

1025 TNTCCAATCCAAAGCTTAAAGTACAGACAGTCCGACTGTTTGACGAATCT 1074
       |||              ::::::  |||      :::
701 erPheAsnLysAspThrThrPheAsnValGluArg......AsnAlaArg 715

1075 TTGAATGAAACTGATAAAGAACCAGTTTACGCGGCAGGGGGTGTTAATCA 1124
     :::|||         |||   |||:::            |||:::|||::
716 ValAsnPheAspIleLysAlaProIle............GlyIleAsnLy 728

1125 GTACCGTCCAAGGTTAAACAACGGTGAAAACCTTTCTTTTATCGATTACG 1174
     :|||                                  |||   ::::::|||:
728 sTyr.............................SerSerLeuAsnTyrA 735

1175 GCAACGGCAAACTCATCTTATCAAACAACATCAACCAAGGCGCGGGCGGT 1224
     :::::          :::::::::|||||||:::   ::::::||||||
735 laSer............PheAsnGlyAsnIleSerValSerGlyGlyGly 747

1225 TTGTATTTTGAAGGTGATTTTACGGTCTCGCCTGAAAACAACGAAACGTG 1274
           :::   ||||||||||:::      :::::::::::::::
748 .........SerValAspPheThrLeuLeuAlaSerSerSerAsnVal.. 760

1275 GCAAGGCGCGGGCGTT.....................CATATCAGTGAAG 1303
      |||      ||||||                    :::::::|||
761 .GlnThrProGlyValValIleAsnSerLysTyrPheAsnValSerThrG 777

1304 ACAGTACCGTTACTTGGAAAGTAAACGGC..................... 1332
       |||::::::   :::|||:::::|||
777 lySerSerLeuArgPheLysThrSerGlySerThrLysThrGlyPheSer 793

1333 GTGGCAAACGAC...CGCCTGTCCAAAATCGGCAAAGGCACGCTGCACGT 1379
     :::   :::|||      |||:::      |||  :::         ::
794 IleGluLysAspLeuThrLeuAsnAlaThrGlyGlyAsnIleThrLeuLe 810

1380 TCAAGCCAAAGGGGAAAAC.........................CAAG 1402
     :|||:::::::|||   :::                        :::
810 uGlnValGluGlyThrAspGlyMetIleGlyLysGlyIleValAlaLysL 827

1403 GCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCAGGCAGAC 1452
       :::|||:::         |||::::::   :::
827 ysAsnIleThrPheGluGlyGlyAsnIleThrPhe.............. 838

1453 GATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGNTCAGCGGCAG 1502
           |||:::::::::|||   :::|||||         :::|||::
839 ......GlySerArgLysAlaValThrGluIle.........GluGlyAs 850

1503 GGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAACTCT 1552
     :   |||:::::::   ||||||:::                        858
850 nValThrIleAsnAsnAsnAlaAsn.......................

1553 ATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCTTTCG 1602
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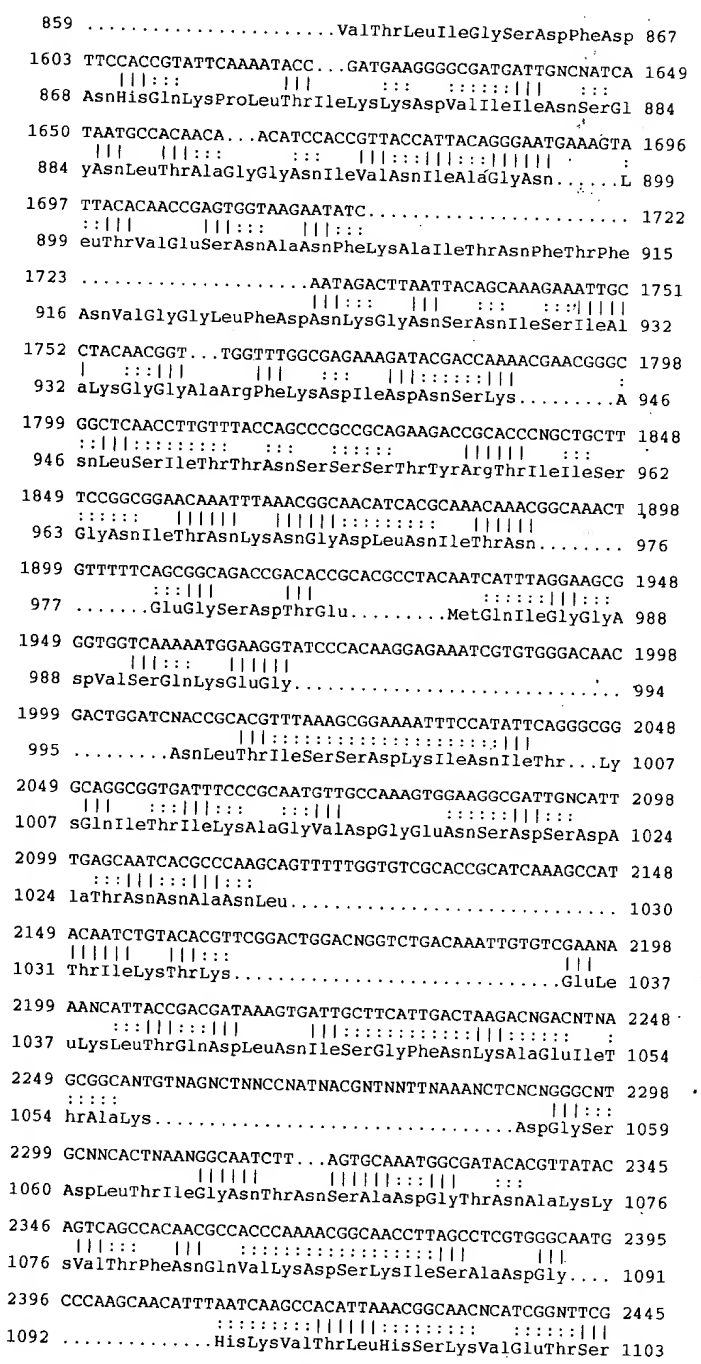

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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1993.DAT:AAR41725

seq_documentation_block:
ID   AAR41725 standard; Protein; 1536 AA.
XX
AC   AAR41725;
XX
DT   26-APR-1994  (first entry)
XX
DE   High molecular weight protein 1 (HMW1).
XX
KW   HMW; high molecular weight protein; virus; vaccine; influenza;
KW   epitope; immunity; haemophilus influenzae; gene cluster.
XX
OS   Haemophilus influenzae.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 668..677
FT                   /note= "Possibly incorrect sequence. Alternative
FT                          sequence for this region is LNVSESGEFN.
FT                          (See comments)."
XX
PN   WO9319090-A.
XX
PD   30-SEP-1993.
XX
PF   16-MAR-1993;   93WO-US02166.
XX
PR   16-MAR-1992;   92GB-0005704.
XX
PA   (BARE/) BARENKAMP S J.
PA   (INRM ) INSERM INST NAT SANTE & RECH MEDICALE.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1993-320683/40.
DR   N-PSDB; AAQ49508.
XX
PT   High molecular weight surface proteins - of non-typeable
PT   haemophilus which exhibit immunogenic properties
XX
PS   Claim 3; Figure 2/10; 100pp; English.
XX
CC   The isolation and purification of the high molecular weight protein
CC   enables the identification of the major protective epitopes of the
CC   protein by conventional epitope mapping.  These epitopes can then be
CC   synthesised using standard techniques and incorporated into fully
CC   synthetic or recombinant vaccines.  This sequence is claimed to be
CC   the same as that given in AAR41723 (High molecular weight protein 1)
CC   although it does differ slightly. (Repeated regions which are
CC   possibly incorrect and occur in the corresponding nucleotide coding
CC   sequence contribute to these differences).
XX
SQ   Sequence   1536 AA;


alignment_scores:
            Quality:  265.00              Length:   1173
              Ratio:  0.457                Gaps:     55
 Percent Similarity:  49.446   Percent Identity: 20.119

alignment_block:
 US-09-303-518D-651 x AAR41725   ..

 Align seg 1/1  to: AAR41725  from: 1  to: 1536

     127 GGACACACTTATTTCGGCATCAACTACCAATACTATCGCGACTTTGCCGA 176
         |||:::||||||:::|||                              :::::
     349 GlyGluThrTyrLeuGly.........................GlyAs 356

     177 AAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTNTACAACA 226
         :::::::|||:::         |||   :::   |||::::::   :::|
     356 pGluArgGlyGlu.........GlyLysAsnGlyIleGlnLeuAlaLysL 370

     227 AAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGAT 276
         ||                        |||:::   |||:::      |||:::
     370 ys.................ThrSerLeuGluLysGlySerThrIleAsn 380

     277 TTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAATA 326
         |||      ::::::::::|||   |||   :::   ||||||
     381 ValSerGlyLysGluLysGlyGlyArgAlaIleValTrpGlyAspIleAl 397

     327 TATTGTG............................AGCGTGGCACATA 346
         :::::::                           :::::::|||   :
     397 aLeuIleAspGlyAsnIleAsnAlaGlnGlySerGlyAspIleAlaLysT 414

     347 ACGGCGGCTAT..............................AACAAC 363
         ::|||||:::                                 :::|||
     414 hrGlyGlyPheValGluThrSerGlyHisAspLeuPheIleLysAspAsn 430

     364 ......GTTGATTTTGGTGCGGAAGGAAGNAATCCCGATCAGCACCGTTT 407
               ||||||                  :::|||||:::      ::
     431 AlaIleValAspAlaLysGluTrpLeuLeuAspProAspAsnValSerIl 447

     408 TTCTTACCAAATTGTGAAAAGAAATAATTATAAGCCTGACAATTCACACC 457
         ::::   :::   :::   |||:::|||   :::   ||||||||||
     447 eAsnAlaGluThrAlaGlyArgSerAsnThrSerGluAspAspGluTyrT 464

     458 CTTACAACGGCGAT...TANCATATGCCGCGTTTGCATAAATTTGTCACA 504
               :::|||:::   :::      |||:::   :::|||      |||
     464 hrGlySerGlyAsnSerAlaSerThrProLysArgAsnLysGluLysThr 480

     505 GATGCAGAACCTGTCGAAATGACGAGTGACATGAGGGGGAATACCTATTC 554
                         :::   :::   |||   ::::::   :::|||:::
     481 ThrLeuThrAsnThrThrLeuGluSerIleLeuLysLysGlyThrPheVa 497

     555 CGATAAAGAAAAATATCCCGAGCGTGTCCGCATCGGCTCAGGACACCAC. 603
         :::                  :::|||:::   :::::::|||:::   :::
     497 lAsnIleThrAla...AsnGlnArgIleTyrValAsnSerSerIleAsnL 513

     604 ...................TATTGGCGTTAT..................... 615
                             |||
     513 euSerAsnGlySerLeuThrLeuTrpSerGluGlyArgSerGlyGlyGly 529

     616 ..............................GATGATGACAAACACGGCGA 635
                                      ||||||   :::   :::::
     530 ValGluIleAsnAsnAspIleThrThrGlyAspAspThrArgGlyAlaAs 546

     636 TTTATCC...TACTCCGGCGCATGGTTA.....................A 661
         :|||:::   ||||||||||:::|||:::                   :
     546 nLeuThrIleTyrSerGlyGlyTrpValAspValHisLysAsnIleSerL 563

     662 TTGGC......GGCAATACACATATGCAGGGT................... 687
         ::|||      ||||||   ::::::   :::
     563 euGlyAlaGlnGlyAsnIleAsnIleThrAlaLysGlnAspIleAlaPhe 579

     688 ...TGGGGAAATAATGGCGTANTTAGTTTGAGCGGCGATGTGCGCCATGC 734
               |||:::|||   |||   :::   ::|||   :::      ::
     580 GluLysGlySerAsnGlnValIleThrGlyGlnGlyThrIleThrSerGl 596

     735 CAACGACTATGGCCCTATGCCGATTGCAGGTGCGGCAGGCGACAGCGGTT 784
         :|||:::   |||                        :::   :::   :::|||||
     596 yAsnGlnLysGlyPheArgPheAsnAsnValSerLeuAsnGlyThrGlyS 613

     785 CGCCAATGTTTATTTATGACAAAACAAACAATAAATGGCTGCTCAACGGA 834
         ||   :::   :::       |||   :::||||||:::   :::::::::
     613 erGlyLeuGlnPheThrThrLysArgThrAsnLysTyrAlaIleThrAsn 629

     835 GTTTTACAAACCGGCTACCCTTATTCCGGCAGGGAAAACGGTTTCCAGCT 884
         ::::::                  |||||||:::   |||       :::::
     630 LysPheGluGlyThrLeuAsnIleSerGlyLysValAsnIleSerMetVa 646

     885 GATACGCAAAGATTGGTTCTACGATGACATTTACAGAGGCGATACACAT. 933
         ::::   |||:::            |||   ::::::|||   |||:::
     646 lLeuProLysAsnGluSerGlyTyrAspLysPheLysGlyArgThrTyrT 663
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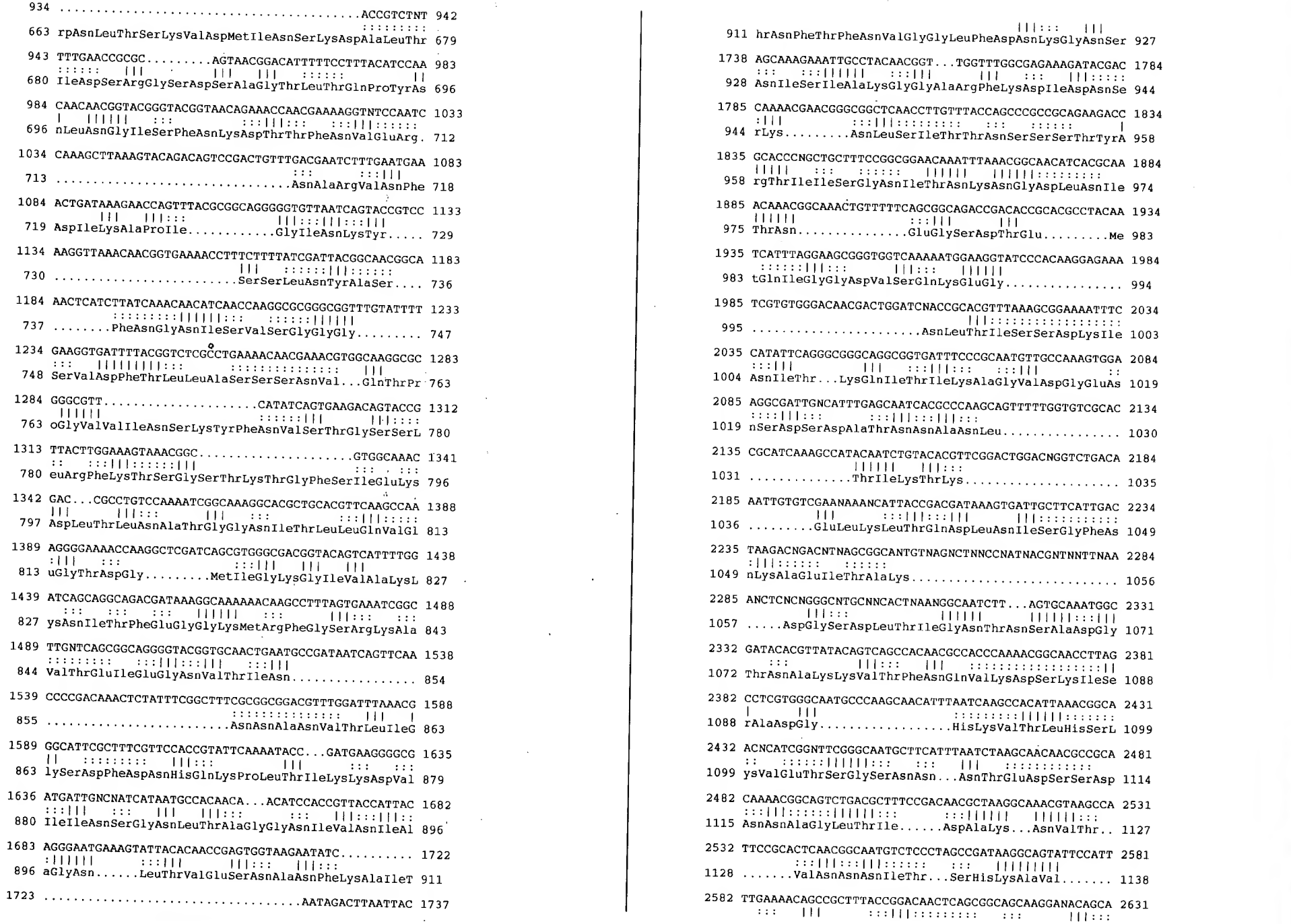

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1139 ..SerIleSerAlaThrSerGlyGluIleThrThrLysThrGlyThrThr 1154

2632 TTACACTTAAAA......GACAGCGAATGGACGCTGCCGTCAGGCACGGA 2675
     ::::::            :::   |||   |||      :::|||:::
1155 IleAsnAlaThrThrGlyAsnValGluIleThrAlaGlnThrGlySerIl 1171

2676 ATTAGGCAATTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCT 2725
     ||||||:::::::::   ::::::::::::::::|||||:::::::::
1171 eLeuGlyGlyIleGluSerSerSerGlySerValThrLeuThrAlaThr. 1187

2726 ATCGCCACGATGCTGCAGGCGCGCAAACCGGCAGNGTGTCAGACACGCCG 2775
           ::::::|||   |||   ::::::      :::::::|||
1188 ........GluGlyAlaLeuAlaValSerAsnIleSerGlyAsnThrVal 1201

2776 CGCCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGT 2825
           ::::::   :::   |||::::::          ::::::::
1202 ThrValThrAlaAsnSerGlyAlaLeuThrThrLeuAlaGlySerThrIl 1218

2826 AGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACNGTCAAG 2875
     :::::::      ::::::   |||   :::   :::   :::     |
1218 eLysGlyThrGluSerValThrThrSerSerGlnSerGlyAspIleGlyG 1235

2876 GAACATTC.....................CGCTTTATGTCGGAACTCTTC 2904
     ||||||:::                   :::      ::::::|||
1235 lyThrIleSerGlyGlyThrValGluValLysAlaThrGluSerLeuThr 1251

2905 GGCTACCGAAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGNACTTA 2954
           ::::::|||:::|||   |||   ::::::|||::::::
1252 ThrGlnSerAsnSerLysIleLys...AlaThrThrGlyGluAlaAsnVa 1267

2955 CACCTTGGCGGTC.....................AACAATACCGGCA 2980
      |||   |||:::                     :::||||||   |
1267 lThrSerAlaThrGlyThrIleGlyGlyThrIleSerGlyAsnThrValA 1284

2981 ACGAACCCGTAAGCCTCGATCAATTGACGGTA..................... 3012
     ||      ::::::     :::||||||||||
1284 snValThrAlaAsnAlaGlyAspLeuThrValGlyAsnGlyAlaGluIle 1300

3013 ......GTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTT 3056
           :::||||||      :::       |||::::::
1301 AsnAlaThrGluGlyAlaAlaThrLeuThrThrSerSerGlyLysLeuTh 1317

3057 CACCCTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACTCA 3106
      |||      :::::::|||:::   ::: |||::::|||   :::|||.
1317 rThrGluAlaSerSerHisIleThrSer.AlaLysGlyGlnValAsnLeu 1333

3107 TCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAG 3156
     ||||||:::   :::|||   |||      |||::::::   |||   ::
1334 SerAlaGlnAspGlySerValAlaGlySerIleAsnAlaAlaAsnValTh 1350

3157 CTTTCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGA 3206
     ::::   |||:::::::::            |||:::   :::   ::::
1350 rLeuAsnThrThrGlyThrLeuThrThrValLysGlySerAsnIleAsnA 1367

3207 CAACGCGCAAAGCCTTG 3223
     ::|||      :::|||
1367 laThrSerGlyThrLeu 1372
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01824

seq_documentation_block:

ID AAB01824 standard; Protein; 1227 AA.
XX
AC AAB01824;
XX
DT 11-SEP-2000 (first entry)
XX
DE Haemophilus influenzae strain Joyc HMW1A protein, SEQ ID NO:26.
XX
KW HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW recombinant production; Escherichia coli; antibacterial; vaccine;
KW human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW detection; diagnosis.
XX
OS Haemophilus influenzae strain Joyc.
XX
PN WO200020609-A2.
XX
PD 13-APR-2000.
XX
PF 07-OCT-1999; 99WO-CA00938.
XX
PR 07-OCT-1998; 98US-0167568.
PR 08-DEC-1998; 98US-0206942.
XX
PA (CONN-) CONNAUGHT LAB LTD.
XX
PI Loosmore SM, Yang Y, Klein MH;
XX
DR WPI; 2000-303789/26.
DR N-PSDB; AAA52175.
XX
PT Nucleic acid molecule for producing recombinant high molecular weight
PT proteins of Haemophilus which are used as a vaccine to provide
PT protection against Haemophilus induced diseases in humans -
XX
PS Claim 12; Fig 18A-R; 307pp; English.
XX
CC The invention relates to the recombinant production of Haemophilus
CC influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC expression construct used to effect recombinant expression comprises a
CC promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC and the hmwB and hmwC genes encode accessory proteins which are
CC responsible for post-translational processing and secretion of the HMWA
CC proteins. The modified hmwABC operon used in the expression construct of
CC the invention contains an A gene modified such that it encodes only the
CC mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC vectors are used for the production of recombinant H. influenzae HMW
CC proteins which can be used as vaccines to mediate a humoral or
CC cell-mediated immune response to provide protection against diseases in
CC humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC antigens in immunoassays for detecting antibodies against Haemophilus,
CC HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC HMW proteins can be used to isolate and clone hmw genes from other
CC non-typeable strains of Haemophilus via hybridisation reactions. The
CC present sequence represents an HMWA protein from a non-typeable strain of
CC H. influenzae.
XX
SQ Sequence 1227 AA;

alignment_scores:

Quality:	264.50	Length:	1161
Ratio:	0.474	Gaps:	62
Percent Similarity:	48.062	Percent Identity:	21.102

alignment_block:
US-09-303-518D-651 x AAB01824 ..

Align seg 1/1 to: AAB01824 from: 1 to: 1227

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 388 AATCCCGATCAGCACCGTTTTTCTTACCAAATTGTGAAAAGAAATAATTA 437
     :::||||||::      ::::::          :::|||||||:::
   6 AspProAspAsnValSerIleAsnAlaGlyThrSerGluArgAsnAspAl 22

 438 TAAGCCTGACAATTCACACCCTTACAAC...GGCGATTANCATATGCCGC 484
      :::|||   ::::::   |||   :::   |||           |||:
  22 aSerProThrGluAspPheProThrGlyAlaGlyGlyLysAspAsnProL 39
```

```
 485 GT.....TTGCATAAA 495
     ::                |||::::::
  39 ysLysAsnAlaHisAsnLysProThrLeuIleAsnThrThrLeuGluArg 55

 496 TTTGTCACAGATGCAGAACCTGTCGAAATGACGAGTGACATGAGGGGGAA 545
     :::::::::          |||::::::|||:::      |||   ::
  56 IleLeuSerGlyAsnThrPheValAsnIleThrAlaArgLysArgIleTh 72

 546 TACCTATTCCGATAAAGAAAAATATCCCGAGCGTGTCCGCATCGGCTCAG 595
     ::::   ||||||                :::::|||   ::::
  72 rValAsnSerAsp.....IleAsnIleLysAspS 82

 596 GACACCAC......TATTGGCGTTATGATGATGACAAACACGGC...GAT 636
     ::   |||       |||     :::|||::::::   ||| ' |||
  82 erSerHisLeuIleLeuTrpSerGluAsnAspAsnSerSerGlyValAsp 98

 637 TTATCC.....TACTC 647
     ::::::          |||||
  99 IleLysGlyAsnIleThrSerThrThrGlyGlySerLeuThrIleTyrSe 115

 648 CGGCGCATGGTTAATTGGCGGCAATACACATATGCAGGGTTGGGGAAATA 697
     |:::::|||:::         :::   |||  :::        |||:
 115 rSerGlyTrpIle.....AspIleHisLysAsnIleThrLeuAsnS 129

 698 ATGGCGTANTTAGTTTGAGC.....GGCGATGTGCGCCATGCCAAC 738
     ::|||:::   :::::::::          |||||||:::        :::
 129 erGlyLeuLeuAsnIleThrThrLysGlnGlyAspIleAlaPheGluLys 145

 739 GACTATGGCCCTATGCCGATTGCAGGT.....GCGGCAGGCGA 776
         :::|||     |||:::|||          :::|||||::
 146 GlyAsnAsnPro...ThrIleThrGlyGlnGlyThrIleThrAlaGlyAs 161

 777 CAGC.....GGTTCGC 787
     ::::              |||:::
 161 nGlyLysGlyPheArgPheGluAsnAlaSerLeuAsnGlyIleGlyThrG 178

 788 CAATGTTTATT.....TATGACAAAACAAACAATAAATGGCTGCTC 828
       :::::::::          |||      ||||||    ::::::
 178 lyLeuLeuPheAsnIleLysArgAspLeuGlyAsnAsnPheGlnIleIle 194

 829 .....AACGGAGTTTTACAAACCGGCTACCCTTATTCCGGCAGGGA 869
           ||||||:::|||:::                  |||||||:::
 195 AsnPhePheAsnGlyThrLeuAsn.....IleSerGlyLysVa 207

 870 AAACGGTTTCCAGCTGATACGCAAAGATTGGTTCTACGATGACATTTACA 919
      |||      ::::::|||   |||   |||   |||:::      :::|
 207 lAsnIleSerMetValIleProLysLysTrpAspTyrSerLys...PheA 223

 920 GAGGCGATACACAT......ACCGTCTNTTTTGAACCGCGCAGTAACGGA 963
     |||||   |||:::      ::::::   ::::::      :::::::::
 223 rgGlyArgThrTyrTrpAsnValThrHisLeuAsnValSerGluGlySer 239

 964 CATTTTTCCTTTACATCCAACAACAACGGTACGGGTACGGTAACAGAAAC 1013
       |||:::::::|||   ::::::::::|||       |||:::
 240 LysPheAsnLeuThrIleAspSerArgGlyAspAspThrAlaGlyThrLe 256

1014 CAACGAAAAGGTNTCCAATCCAAAGCTTAAAGTACAGACAGTCCGACTGT 1063
      |||         :::         ::::::   :::      , :::|
 256 uAsnThrProTyrAsnLeuAsnGlyIleSerPheAsnLysAspThrIleP 273

1064 TTGACGAATCTTTGAATGAAACTGATAAAGAACCAGTTTACGCGGCAGGG 1113
     |||||   :::   |||  :::          :::   |||
 273 heAspValLysGlnAsnGlyAlaValThrPheAspIleLysAlaProIle 289

1114 GGTGTTAATCAGTACCGTCCAAGGTTAAACAACGGTGAAAACCTTTCTTT 1163
     ||||||                    ||||||::::::||||||:::::
 290 GlyVal.....AsnAsnAsnArgAsnLeuAsnTy 299

1164 TATCGATTACGGCAACGGCAAACTCATCTTATCAAACAACATCAACCAAG 1213
     :   ::::::   ||||||::::::   :::|||                |
 299 rAlaSerPhe...AsnGlyAsnIleSerValSer.....G 310
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```
1214 GCGCGGGCGGTTTGTATTTTGAA..... 1236
     ||:::|||::::::   |||:::
 310 lyGlyGlyAsnValThrPheLysLeuLeuAlaSerSerSerThrAlaGln 326

1237 ......GGTGATTTTACGGTCTCGCCTGAAAACAACGAAACGTGGCAAGG 1280
           |||   |||      |||   :::   |||   :::      ::
 327 ThrProGlyValPheIleAsnSerLysHisPheAsnAlaSerGlyGlySe 343

1281 CGCGGGCGTTCATATCAGTGAAGACAGTACCGTTACTTGGAAAGTAAACG 1330
     ::::             :::|||   ||||||         ||||||:::
 343 rSerLeuGluPheArgThrGluGlySerThr.....LysValGlyP 357

1331 GCGTGGCAAACGACCGCCTGTCC..... 1353
       :::   |||:::   |||:::
 357 heLeuIleAsnAsnAspLeuThrLeuAsnAlaThrGlyGlyAsnIleSer 373

1354 .....AAAATCGGCAAAGGCACGCTGCA 1376
                              ||||||||||||
 374 LeuLeuGlnValGluGlyIleAspGlyMetIleGlyLysGly..... 387

1377 CGTTCAAGCCAAAGGGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGTA 1426
      |||   ||||||                 :::|||:::   :::   |||:
 388 .ValValAlaLys.....LysAsnIleThrPheAlaGlyGlyA 400

1427 CAGTCATTTTGGATCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTT 1476
     :::::   :::                    |||:::|||:::|||:::
 400 snIleThrPhe.....GlySerLysLysAlaIle 409

1477 AGTGAAATCGGCTTGNTCAGCGGCAGGGGTACGGTGCAACTGAATGCC.. 1524
     :::||||||          :::|||:::::|||:::::   ||||||
 410 ThrGluIle.....GluGlyAsnAlaThrIleAsnAsnAsnAlaAs 423

1525 .....GATAATCAGTTCAACCCC..... 1542
                          ||||||:::   :::|||
 423 nValThrLeuIleGlySerAspPheAspAsnHisGlnLysProLeuThrI 440

1543 ........GACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTA 1584
           |||   :::          :::::::::|||:::|||
 440 leLysLysAspValIle.....IleAsnSerGlyAsnLeuThrAla 453

1585 AACGGGCATTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGC 1634
     :::|||:::   ::::::::::::          :::::::::::|||||
 454 GlyGlyAsnValIleAsnIleAsnGlyAsnLeuThrValAsnAsnGlyAl 470

1635 GATGATTGNCNATCATAATGCCACAACAACATCCACCGTTACCATT.... 1680
     |   :::          :::|||   |||:::   |||   ::::::
 470 aAsnLeu.....LysAlaIleThrAsnPheThrPheAsnValGlyG 484

1681 ..............ACAGGGAATGAAAGTATTACACAACCGAGTGGT... 1713
                          ||||||:::::|||:::          |||
 484 lyLeuPheAspAsnLysGlyAsnSerAsnIleSerIleAlaArgGlyGly 500

1714 .........AAGAATATCAATAGACTTAATTACAGCAAAGAAATTGCCTA 1754
             |||:::||||||:::   :::   |||   :::|||:::
 501 AlaLysPheLysAspIleAsnAsnThrSer...SerLeuAsnIleThrTh 516

1755 CAACGGTTGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGCGGCTCA 1804
      |||                :::|||||||||
 516 rAsn.....SerAspThrThr..... 521

1805 ACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCNGCTGCTTTCCGGC 1854
           |||:::         |||   :::   ::       :::|||
 522 ........TyrArgThrIleIleGluGlyAsnIleThrAsnLysAlaGly 535

1855 GGAACAAAT.....TTAAACGG 1871
         |||                          :::::::||
 536 AspLeuAsnIleIleAspAsnLysGlyAsnAlaGluIleGlnIleGlyGl 552

1872 CAACATCACGCAAACAAACGGCAAACTGTTTTTCAGCGGCAGACCGA... 1918
     |||||||:::|||   :::|||:::|||   :::||| :::|||:::
 552 yAsnIleSerGlnLysGluGlyAsnLeuThrIleSer.SerAspLysIle 568

1919 CACCGCACGCCTACAATCATTTAGGAAGCGGGTGGTCAAAAATGGAAGGT 1968
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 569 AsnIleThrAsnGlnIleThrIleLysLysGly..... 579

1969 ATCCCACAAGGAGAAATCGTGTGGGACAACGACTGGATCNACCGC....A 2014
 580 .ValAsnLysGluAspSerAspSerSerThrAlaAsnAsnAlaAsnLeuT 596

2015 CGTTTAAAGCGGAAAATTTCCATATTCAGGGCGGGCAGGCGGTGATTTCC 2064
 596 hrIleLysThrLysGluLeuGlnLeuThrGlyAspLeuAsnIleSerGly 612

2065 CGCAATGTTGCCAAAGTGGAA.....GG 2087
 613 PheAspLysAlaGluIleThrAlaLysGluGlyAlaAspLeuIleIleGl 629

2088 CGATTGNCATTTGAGCAATCACGCCCAAGCA.....GTTTTTGGTG 2128
 629 yAsnSerAspAsnAsnAsnAsnAlaAsnAlaLysLysValThrPheAsnG 646

2129 TCGCACCGCATCAA.....AGCCATACAATCTGTACACGT 2163
 646 lnValLysAspSerLysIleSerAlaGlySerHisAsnValThrLeuAsn 662

2164 TCG..... 2166
 663 SerLysValGluThrSerAsnGlyAsnAsnAspAlaGluSerAsnAsnGl 679

2167 .GACTGGACNGGTCTGACA.....AATTGTGTCGAANAAA 2200
 679 yAspSerThrSerLeuThrIleAsnAlaLysAsnValThrValAsnAsnA 696

2201 NCATTACCGACGATAAAGTGATT..... 2223
 696 snIleThrSerHisLysThrValAsnIleThrAlaSerGluAsnValThr 712

2224 ......GCTTCATTGACTAAGACNGACNTNAGCGGCANTGTNAGNCTNNC 2267
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2268 CNATNACGNTNNTTNAAANCTCNCNGGGCNTGCNNCACTNAANGGC.... 2313
 729 rAlaLysThrGlyAspIleLysGlyGlyIleGluSerAsnSerGlyAsnV 746

2314 ..AATCTTAGTGCAAATGGCGATACACGTTATACAGTCAGCCACAACGCC 2361
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2362 ACCCAAAACGGCAACCTT..... 2379
 762 GlyGlnAsnValThrValAlaAlaAlaSerGlyAlaValThrThrThrLy 778

2380 .....AGCCTCGTGGGCAATGCCCAAGCAACATTTAATC 2413
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2414 AAGCCACATTAAACGGC.....AACNCA 2436
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2437 TCGGNTTCGGGCAATGCTTCATTTAATCTAAGCAACAACGCCGCACAAAA 2486
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2487 CGGCAGTCTGACGCTTTCCGACAACGCTAAGGCAAACGTAAGCCATTCCG 2536
 828 nValThrValThrAlaAsnSerGlyAlaIleThrThrThrGluGlySerT 845

2537 CACTCAAC.....GGCAATGTCTCCCTAGCCGATAAGGCAGTATTC 2577
 845 hrIleAsnAlaThrThrGlyAspAlaAsnIleThrThrGln..... 858

2578 CATTTTGAAAACAGCCGCTTTACCGGACAACTCAGCGGCAGCAAGGANAC 2627
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 859 .....ThrGlyAsnIleAsnGlyLysValGluSe 868

2628 AGCATTACACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAAT 2677
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2678 TA......GGCAATTTAAACCTTGACAACGCCACCATTACACTCAAT... 2718
 882 euAlaValGlyAsnIleSerGlyAspThrValThrIleThrAlaAspLys 898

2719 .....TCCGCCTATCGCCACGA 2735
 899 GlyLysLeuThrThrGlnThrSerSerLysIleAsnGlyThrLysServa 915

2736 TGCTGCAGGCGCGCAAACCGGCAGNGTGTCAGACACGCCGCGCCGCCGTT 2785
 915 lThrThrSerSerGlnSerGlyAspIleSerGlyThr..... 927

2786 CGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAATCCCGT 2835
 928 .....IleSerGlyAsn 931

2836 TTCAACACGCTGACGGTAAACGGCAAATTGAACNGTCAAGGAACATTCCG 2885
 932 ThrValSerValSerAlaThrGlySerLeuThrThrGlnAla..... 945

2886 CTTTATGTCGGAACTCTTCGGCTACCGAAGCGACAAATTGAAGCTGGCGG 2935
 946 .....GlySerLysIleGlu...AlaL 952

2936 AAAGTTCCGAAGGNACTTACACCTTGGCGGTC..... 2967
 952 ysThrGlyGluAlaAsnValThrSerAlaThrGlyThrIleGlyGlyThr 968

2968 ......AACAATACCGGCAACGAACCCGTAAGCCTCGATCAATTGACGGT 3011
 969 IleSerGlyAsnThrValAsnValThrAlaAsnThrAspAsnLeuThrIl 985

3012 AGTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTC.... 3057
 985 eLysAspGlyAlaArgIleLysAlaThrGlyGlyAlaValThrLeuThrA 1002

3058 ...........ACCCTGCAAAACGAACACGTCG.....ATGCCGGC 3087
1002 laThrGlyGlyThrLeu.ThrThrGluThrSerSerAspIleThrSerSe 1018

3088 GCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGCATAA 3137
1018 rAsnGlyGlnThrThrLeuThrAlaLysAspSerSerIleAlaGlySerI 1035

3138 TCCGGTCAAAGAACAAGAGCTTTCCGACA 3166
1035 leAsnAlaAlaAsnValThrLeuAsnThr 1044
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01830

seq_documentation_block:
ID   AAB01830 standard; Protein; 1222 AA.
XX
AC   AAB01830;
XX
DT   11-SEP-2000  (first entry)
XX
DE   H. influenzae strain K1 mature full-length HMW1A protein, SEQ ID NO:37.
XX
KW   Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain K1.
XX
```

```
FH   Key             Location/Qualifiers
FT   Misc-difference 307
FT                   /note= "Encoded by GG"
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52180.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 8; Fig 20A-R; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   1222 AA;
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alignment_scores:
            Quality:  264.00              Length:   1325
              Ratio:  0.401                Gaps:     60
 Percent Similarity:  49.736   Percent Identity: 20.377

alignment_block:
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       3 AsnValSerIleAsnAlaProAlaLeuGlyArgThrGluSerThrProAs 19

     396 TCAGCACCGTTTTTCTTACCAAATTGTGAAAAGAAATAATTATAAGCCTG 445
         :::::::      :::|||:::      ::::::   |||||||||
      19 nAsnAsn......GluTyrAspSerProAsnGlnIleAsnTyrLysAsnL 34

     446 ACAATTCACACCCTTACAACGGCGATTANCATATGCCGCGTTTGCATAAA 495
         |||                     ::::::   :::   |||:::   |||
      34 ysProSerLeuSerThrLeuThrAsnThrThrLeuGluArgIleLeuLys 50

     496 TTTGTCACAGATGCAGAACCTGTCGAAATGACGAGTGACATGAGGGGGAA 545
           |||:::         |||:::::::|||:::             ::
      51 ArgAsnThrSer.........ValAsnIleThrAlaThrLysThrIleTh 64

     546 TACCTATTCCGATAAAGAAAAATATCCCGAGCGTGTCCGCATCGGCTCAG 595
         ::::   ||||||                        ::::::||||||::::
      64 rValAsnSerAsp.....................IleAsnIleGlyAspS 74

     596 GACACCACTATTGGCGTTATGATGATGACAAA..................... 627
         ::   |||         :::::::::   :::
      74 erSerHisLeuThrLeuTrpSerGluGlyGlnGlyArgGlyGlyValAsn 90

     628 ..........................CACGGCGATTTATCC...TACTC 647
                                  :::|||:::|||:::   |||||
      91 ValThrGlyAsnIleThrSerThrThrAsnGlyAsnLeuThrIleTyrSe 107

     648 CGGCGCATGGTTA...ATTGGCGGCAATACACATATGCAGGGTTGGGGAA 694
         ||||:::|||:::   :::      |||      :::::::::   |||
     107 rGlyGlyTrpValAspValHisLysAsnIleThrLeuLysSer...GlyT 123

     695 ATAATGGCGTANTTAGTTTGAGCGGCGATGTGCGCCATGCCAACGACTAT 744
         :::::::::::   :::|||||||:::          :::
     123 yrLeuAsnIleThrThrLysGlnGlyAspIleAlaPheGluAspLysPro 139

     745 GGC.............CCTATGCCGATTGCAGGTGCGGCAGGCGACAGCGG 782
         |||                 :::         |||:::   :::   :::::
     140 GlyLeuSerAsnLeuThrIleThrAlaLysGlyThrIleAlaValAsnAs 156

     783 TTCGCCAATGTTTATTTATGACAAAACAAACAATAAATGGCTGCTCAACG 832
         ::::      |||   :::|||:::::::::            |||||||
     156 nLysLysGlyPheArgPheAspAsnValThr.............LeuAsnG 169

     833 GAGTT.......................TTACAAACCGGCTACCCTTAT 858
         ||:::                       ::::::||||||
     169 lyThrGlyGlyGlyLeuSerPheLysTyrIleGluThrGlyAsnArgAsp 185

     859 TCCGGCAGGGAAAACGGTTTC............................. 879
         |||:::   |||:::   |||
     186 SerAsnPheGluThrHisPheArgGlyArgLeuAsnIleSerGlyLysVa 202

     880 .............CAGCTGATACGCAAAGATTGGTTCTACGATGACATTT 916
                     |||      :::::::::|||
     202 lAspIleLeuMetGlnAlaArgGlnGluAsnTrpAsnArgArgHisTrpG 219

     917 ACAGAGGCGATACACATACCGTCTNTTTTGAACCGCGCAGTAACGGACAT 966
           |||:::      :::::::::   ::::::      :::|||::::::
     219 lyArgSerHisTrpAsnValThrArgLeuAsnValSerGluAsnSerTyr 235

     967 TTTTCCTTTACATCCAACAACAACGGTACGGGTACGGTAACAGAAACCAA 1016
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     236 PheAsnValThrIleAspSerSerGlySer..................... 245

    1017 CGAAAAGGTNTCCAATCCA.........AAGCTTAAAGTACAGACAGTCC 1057
                ::::|||:::|||            |||::::::|||:::
     246 .......AlaSerSerProGlyAlaGlyProLeuAsnAlaGlnSer...G 259

    1058 GACTGTTTGACGAATCTTTGAATGAAACTGATAAAGAACCAGTTTACGCG 1107
           |||         |||:::|||:::                 :::   |||
     259 lyLeuAsnGlyIleSerPheAsnAsnAspThrValPheAsnIleAlaAla 275

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         :::::::::||||||   :::   :::|||   :::
     276 SerSerAlaValAsnPheAsnIleLysProProIle.............. 287

    1155 CCTTTCTTTTATCGATTACGGCAACGGCAAACTCATCTTATCAAACAACA 1204
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     288 .ValAspLysValThrAsnGlyAsnHisThrLeuPheLysGlyAsnIleS 304
```

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1205 TCAACCAAGGCGCGGGCGGTTTGTATTTTGAAGGTGATTTTACGGTCTCG 1254
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 304 erValLeuGlyGlyGlyAspValAsnPheHis......PheAsnAlaSer 318

1255 CCTGAAAACAACGAAACGTGGCAAGGCGCGGGCGTTCATATCAGTGAAGA 1304
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 319 SerSerAsnTyrGlnThrTyr.........GlyValIleIleGluSerGl 332

1305 CAGTACCGTTACTTGGAAAGTAAACGGCGTGGCAAACGACCGCCTGTCCA 1354
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 332 nAsn..............PheSerAlaSerGlyGlySerSerLeuLysP 344

1355 AAATCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGGGAAAACCAAGGC 1404
           ::::::|||:::   |||:::              :::|||:::
 344 heLysSerGluGlySerThrHisAlaAlaPheThrIleLysAsnAspLeu 360

1405 TCGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCAGGCA..... 1449
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1450 .GACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGNTCAGCG 1498
      |||::::::   ||||||:::   :::::::::   :::::::::
 377 eAspSerAsnLeuLysLysSerLeuIleAlaAsnLysAsnIleThrPheG 394

1499 GCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAA 1548
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 394 luGlyGlyAsnIleThrLeuAlaAla..................AspLys 404

1549 CTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCT 1598
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1599 TTCGTTCCACCGTATTCAA...AATACCGATGAAGGGGCGATGATTGNCN 1645
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 421 lThrLeuArgSerAlaAsnTyrGlyAsnAspLysSerAlaLeuSerIleA 438

1646 ATCATAATGCCACAACAACATCCACCGTTACCATTACAGGGAAT...... 1689
        |||:::|||:::   :::::::::|||:::|||||||:::
 438 rgGlyAsnValThrAsnLysGlyAsnLeuThrValThrGlySerAlaIle 454

1690 .........GAAAGTATTACA...CAACCGAGTGGTAAGAATATCAATAG 1727
           :::::::::|||   :::   |||:::|||   :::   ::
 455 AsnIleGluLysAsnLeuThrValGluGlySerAlaLysPheLeuAlaAs 471

1728 ACTTAATTACAGCAAAGAAATTGCCTACAACGGTTGGTTTGGCGAG.... 1773
     :   |||||||||   ::::::      :::|||   |||   :::
 471 nProAsnTyrSerPheAsnVal......SerGlyLeuPheAspAsnGlnG 486

1774 ........................................AAAGATACG 1782
                                              ||||||
 486 lyLysSerAsnIleSerIleAlaLysGlyGlyAlaIlePheLysAspIle 502

1783 ACCAAAACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGA 1832
         :::|||   |||   ||||||::::::   :::      ::::::
 503 GluAsnThr...GlySerLeuAsnIleThrThrLysSerAspSerAsnHi 518

1833 CCGCACCCNGCTGCTTTCCGGCGGAACAAATTTAAACGGCAACATCACGC 1882
       :::|||   :::   ::::::   ||||||   :::|||:::::::::
 518 sHisThrIleIleLysGlyAsnIleThrAsnArgLysGlyAspLeuAsnI 535

1883 AAACAAACGGCAAACTGTTTTTCAGCGGCAGACCGACACCGCACGCCTAC 1932
        ||||||                :::|||      |||
 535 leThrAsn...............AsnGlyAspAsnThrGlu......... 543

1933 AATCATTTAGGAAGCGGGTGGTCAAAAATGGAAGGTATCCCACAAGGAGA 1982
        ::::::|||::::::   |||:::   |||         |||::
 544 IleGlnIleGlyGlyAsnIleSerGlnLysGlu............GlyAs 556

1983 AATCGTGTGGGACAACGACTGGATCNACCGCACGTTTAAAGCGGAAAATT 2032
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 556 nLeuThrIleSerSerAspLysValAsnIleThr.........GluArgI 570

2033 TCCATATTCAGGGCGGG................................. 2049

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 570 leThrIleLysAlaGlyValAsnGlyAspAsnSerAspSerAsnGluAla 586

2050 .........CAGGCGGTGATTTCCCGCAATGTTGCCAAAGTGGAAGGCGA 2090
            :::   :::|||:::   :::       |||:::   :::||
 587 ThrSerAlaAsnLeuThrIleLysThrLysGluLeuLysLeuThrAsnAs 603

2091 TTGNCATTTGAGCAATCACGCCCAAGCAGTTTTGGTGTCGCACCGCATC 2140
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2141 AAAGCCATACAATCTGTACACGTTCGGACTGGACNGGTCTGACAAATTGT 2190
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2230 ...............TTGACTAAGACNGACNTNAGCGGCANTGTNAGNC 2263
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2264 TNNCCNATNACGNTNNTTNAAANCTCNCNGGGCNTGCNNCACTNAANGGC 2313
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2314 AATCTTAGTGCAAATGCGCGAT..................ACACGTTATAC 2345
     |||:::::::::|||::::::                  ::::::   ||
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2346 AGTCAGCCACAACGCCACCCAAAACGGCAACCTTAGCCTC.........G 2386
     |:::|||:::|||:::|||   :::::::::   ::::::          :
 702 rAlaSerGluAsnValThrThrLysAlaGlyThrThrIleAsnAlaThrT 719

2387 TGGGCAATGCCCAAGCAACATTTAATCAAGCCACATTAAACGGCAAC... 2433
     ::|||::::::::::::|||   :::   :::   ::::::|||:::
 719 hrGlySerValGluValThrAlaLysThrGlyAspIleLysGlyGlyIle 735

2434 NCATCGGNTTCGGGCAATGCT.....................TCATTTAA 2462
        |||   |||||||||:::                      :::::||
 736 GluSerAsnSerGlyAsnValAsnIleThrAlaSerGlyAspThrLeuAs 752

2463 TCTAAGCAACAACGCCGCACAAAACGGCAGTCTGACGCTTTCCGACAACG 2512
     |:::||||||   ::::::||||||   :::::::::   :::::::::|
 752 nValSerAsnIleThrGlyGlnAsnValThrValAlaAlaAlaSerGlyA 769

2513 CTAAGGCAAACGTAAGCCATTCCGCACTCAAC.........GGCAATGTC 2553
     ||   ::::::::::::   |||::::::|||          ||||||:::
 769 laValThrThrThrLysGlySerThrIleAsnAlaThrThrGlyAsnAla 785

2554 TCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAACAGCCGCTTTACCGG 2603
     :::::::::   |||                            |||||
 786 AsnIleThrThrLys............................ThrGl 792

2604 ACAACTCAGCGGCAGCAAGGANACAGCA.........TTACACTTAAAAG 2644
     |:::::::::|||:::      :::|||         :::::::::
 792 yGluIleAsnGlyGluValLysSerAlaSerGlyAsnValAsnIleThrA 809

2645 ACAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTT 2694
       |||      ||||||                 :::::::::|||:::::
 809 laSerGlyAsnThrLeu...........AsnValSerAsnIleThrGly 821

2695 GACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCTGCAGG 2744
     :::|||:::|||:::|||   ||||||
 822 GlnAsnValThrValThrAlaAsnSer....................... 830

2745 CGCGCAAACCGGCAGNGTGTCAGACACGCCGCGCCGCCGTTCGCGCCGTT 2794
                |||:::::::::   |||
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2795 CCCTATTATCCGTTACACCGCCAACTTCGGTAGAATCCCGTTTCAACACG 2844
             |||:::         |||:::   :::::::::::::::|||
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2845 CTGACG......GTAAACGGCAAATTGAACNGTCAAGGAACATTCCGCTT 2888
       |||       :::|||||||||:::
 853 GlnThrGlyAsnIleAsnGlyLysVal..................... 861

2889 TATGTCGGAACTCTTCGGCTACCGAAGCGACAAATTGAAGCTGGCGGAAA 2938
                                                   ||||
 862 ..............................................GluS 863

2939 GTTCCGAAGGNACT.....................TACACCTTGGCGGTC 2967
     |||||:::|||:::                     ||||||||||||
 863 erSerSerGlySerValThrLeuIleAlaThrGlyGlnThrLeuAlaVal 879

2968 AACAATACCGGCAACGAACCCGTAAGCCTCGATCAATTGACGGTAGTGGA 3017
     :::|||   :::::::::   |||:::         :::|||:::   ::
 880 GlyAsnIleSerGlyAspThrValThr.........IleThrAlaAspLy 893

3018 AGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAA 3067
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 893 sGlyLysLeuThrThrGlnThrSerSerLysIleAsn............. 905

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3118 GGCGAGTTCCGC.........CTGCATAATCCGGTCAAAGAACAAGAGCT 3158
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 917 GlyAspIleSerGlyThrIleSerGlyAsnThrValSerValSerAlaTh 933

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3209 ACGCGCAAAGCCTTGACGCGCTGATTGCGGCCGGGCGCGATGCCGCCGAA 3258
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 978 uThrIle.....................................LysA 982

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3509 CCAATAGCGGTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTTTTCGCC 3558
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1124 yValGluIleAspValLysTyrIleGlnProGlyIleAlaSerValAsnG 1141

3888 CGGCATCGGAGGCAAAATCCGCC 3910
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1141 luValIleGluAlaLysArgAla 1148
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seq_documentation_block:
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AC   AAB01828;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain K1 full-length HMW1A protein, SEQ ID NO:34.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain K1.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 313
FT                   /note= "Encoded by GG"
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PN   WO200020609-A2.
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PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
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PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52179.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 12; Fig 20A-R; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
```

CC hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC and the hmwB and hmwC genes encode accessory proteins which are
CC responsible for post-translational processing and secretion of the HMWA
CC proteins. The modified hmwABC operon used in the expression construct of
CC the invention contains an A gene modified such that it encodes only the
CC mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC vectors are used for the production of recombinant H. influenzae HMW
CC proteins which can be used as vaccines to mediate a humoral or
CC cell-mediated immune response to provide protection against diseases in
CC humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC antigens in immunoassays for detecting antibodies against Haemophilus,
CC HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC HMW proteins can be used to isolate and clone hmw genes from other
CC non-typeable strains of Haemophilus via hybridisation reactions. The
CC present sequence represents an HMWA protein from a non-typeable strain of
CC H. influenzae.
XX
SQ Sequence 1228 AA;

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Ratio: 0.401 Gaps: 60
Percent Similarity: 49.736 Percent Identity: 20.377

alignment_block:
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Align seg 1/1 to: AAB01828 from: 1 to: 1228

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446 ACAATTCACACCCTTACAACGGCGATTANCATATGCCGCGTTTGCATAAA 495
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 40 ysProSerLeuSerThrLeuThrAsnThrThrLeuGluArgIleLeuLys  56

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546 TACCTATTCCGATAAAGAAAAATATCCCGAGCGTGTCCGCATCGGCTCAG 595
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596 GACACCACTATTGGCGTTATGATGATGACAAA..................  627
    ::   |||         :::::::::   :::
 80 erSerHisLeuThrLeuTrpSerGluGlyGlnGlyArgGlyGlyValAsn  96

628 ..........................CACGGCGATTTATCC...TACTC  647
                               :::|||:::|||:::   |||||
 97 ValThrGlyAsnIleThrSerThrThrAsnGlyAsnLeuThrIleTyrSe 113

648 CGGCGCATGGTTA...ATTGGCGGCAATACACATATGCAGGGTTGGGGAA 694
    ||||:::|||:::   :::     |||      :::::::::   |||
113 rGlyGlyTrpValAspValHisLysAsnIleThrLeuLysSer...GlyT 129

695 ATAATGGCGTANTTAGTTTGAGCGGCGATGTGCGCCATGCCAACGACTAT 744
        ::::::::::::   :::|||||:::          :::
129 yrLeuAsnIleThrThrLysGlnGlyAspIleAlaPheGluAspLysPro 145

745 GGC............CCTATGCCGATTGCAGGTGCGGCAGGCGACAGCGG 782
    |||             :::         |||:::   :::   :::::
146 GlyLeuSerAsnLeuThrIleThrAlaLysGlyThrIleAlaValAsnAs 162

783 TTCGCCAATGTTTATTTATGACAAAACAAACAATAAATGGCTGCTCAACG 832
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162 nLysLysGlyPheArgPheAspAsnValThr............LeuAsnG 175

833 GAGTT.......................TTACAAACCGGCTACCCTTAT 858
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859 TCCGGCAGGGAAAACGGTTTC............................ 879
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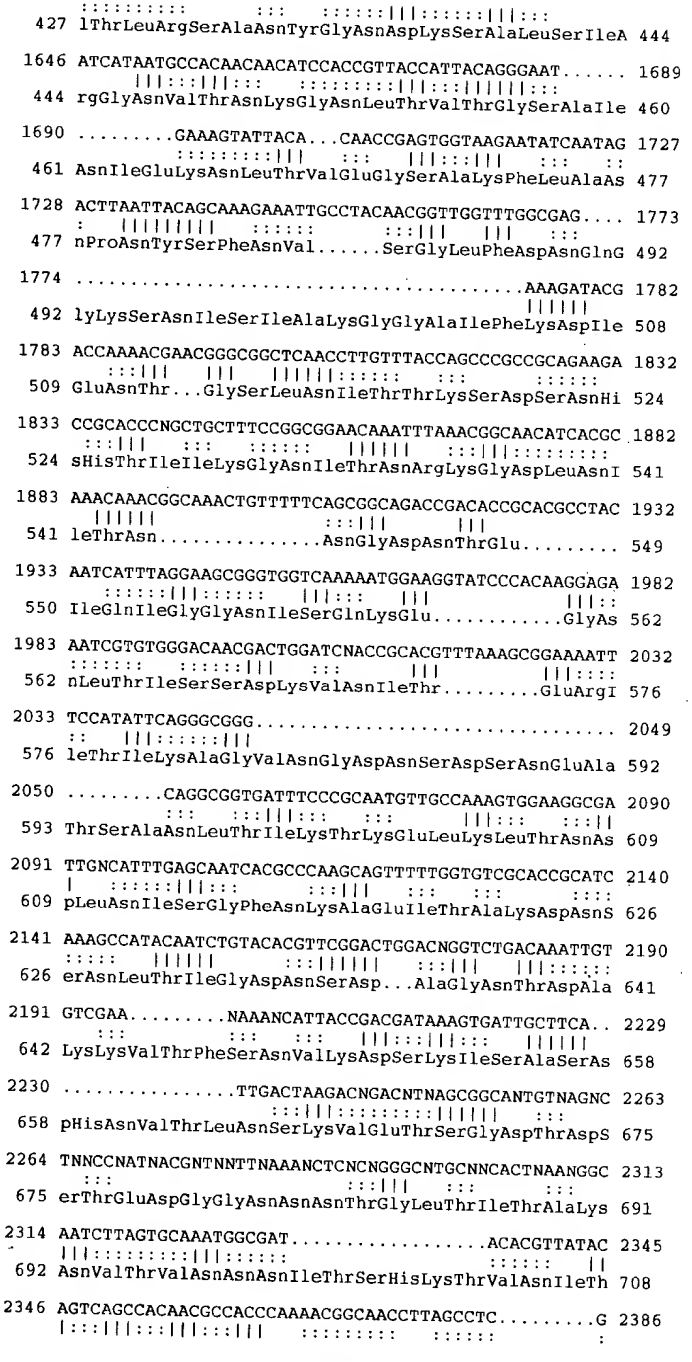
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1728 ACTTAATTACAGCAAAGAAATTGCCTACAACGGTTGGTTTGGCGAG.... 1773
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1833 CCGCACCCNGCTGCTTTCCGGCGGAACAAATTTAAACGGCAACATCACGC 1882
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859 GlnThrGlyAsnIleAsnGlyLysVal..... 867
2889 TATGTCGGAACTCTTCGGCTACCGAAGCGACAAATTGAAGCTGGCGGAAA 2938
868 .....GluS 869
2939 GTTCCGAAGGNACT.....TACACCTTGGCGGTC 2967
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2968 AACAATACCGGCAACGAACCCGTAAGCCTCGATCAATTGACGGTAGTGGA 3017
886 GlyAsnIleSerGlyAspThrValThr.....IleThrAlaAspLy 899
3018 AGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAA 3067
899 sGlyLysLeuThrThrGlnThrSerSerLysIleAsn..... 911
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XX
AC   AAB01825;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain Joyc mature HMW1A protein, SEQ ID NO:28.
XX
KW   Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain Joyc.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52176.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 8; Fig 18A-R; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   1221 AA;
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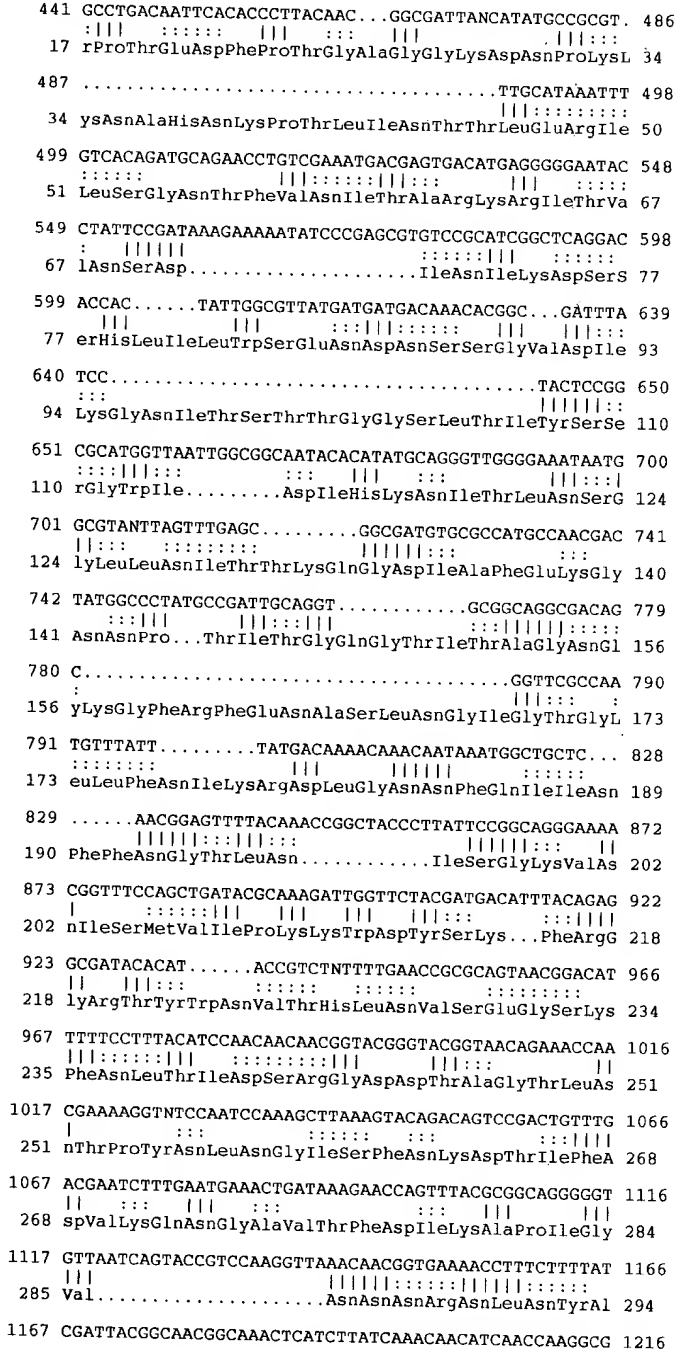
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599 ACCAC.....TATTGGCGTTATGATGATGACAAACACGGC...GATTTA 639
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110 rGlyTrpIle.....AspIleHisLysAsnIleThrLeuAsnSerG 124
701 GCGTANTTAGTTTGAGC.....GGCGATGTGCGCCATGCCAACGAC 741
124 lyLeuLeuAsnIleThrThrLysGlnGlyAspIleAlaPheGluLysGly 140
742 TATGGCCCTATGCCGATTGCAGGT.....GCGGCAGGCGACAG 779
141 AsnAsnPro...ThrIleThrGlyGlnGlyThrIleThrAlaGlyAsnGl 156
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285 Val.....AsnAsnAsnArgAsnLeuAsnTyrAl 294
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1284 GGGCGTTCATATCAGTGAAGACAGTACCGTTACTTGGAAAGTAAACGGCG 1333
338 rLeuGluPheArgThrGluGlySerThr.....LysValGlyPheL 352
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405 GluIle.....GluGlyAsnAlaThrIleAsnAsnAsnAlaAsnVa 418
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2018 TTAAAGCGGAAAATTTCCATATTCAGGGCGGGCAGGCGGTGATTTCCCGC 2067
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AC AAB01826;
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DT 11-SEP-2000 (first entry)
XX
DE Haemophilus influenzae strain Joyc HMW2A protein, SEQ ID NO:30.
XX
KW HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW recombinant production; Escherichia coli; antibacterial; vaccine;
KW human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW detection; diagnosis.

XX
OS Haemophilus influenzae strain Joyc.
XX
PN WO200020609-A2.
XX
PD 13-APR-2000.
XX
PF 07-OCT-1999; 99WO-CA00938.
XX
PR 07-OCT-1998; 98US-0167568.
PR 08-DEC-1998; 98US-0206942.
XX
PA (CONN-) CONNAUGHT LAB LTD.
XX
PI Loosmore SM, Yang Y, Klein MH;
XX
DR WPI; 2000-303789/26.
DR N-PSDB; AAA52177.
XX
PT Nucleic acid molecule for producing recombinant high molecular weight
PT proteins of Haemophilus which are used as a vaccine to provide
PT protection against Haemophilus induced diseases in humans -
XX
PS Claim 12; Fig 19A-O; 307pp; English.
XX
CC The invention relates to the recombinant production of Haemophilus
CC influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC expression construct used to effect recombinant expression comprises a
CC promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC and the hmwB and hmwC genes encode accessory proteins which are
CC responsible for post-translational processing and secretion of the HMWA
CC proteins. The modified hmwABC operon used in the expression construct of
CC the invention contains an A gene modified such that it encodes only the
CC mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC vectors are used for the production of recombinant H. influenzae HMW
CC proteins which can be used as vaccines to mediate a humoral or
CC cell-mediated immune response to provide protection against diseases in
CC humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC antigens in immunoassays for detecting antibodies against Haemophilus,
CC HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC HMW proteins can be used to isolate and clone hmw genes from other
CC non-typeable strains of Haemophilus via hybridisation reactions. The
CC present sequence represents an HMWA protein from a non-typeable strain of
CC H. influenzae.
XX
SQ Sequence 975 AA;

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Ratio: 0.498 Gaps: 54
Percent Similarity: 43.568 Percent Identity: 19.253

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US-09-303-518D-651 x AAB01826 ..

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 104 ThrSerThr....................................... 106

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1403 GCTCGATCAGCGTGGGC.....................GACGGTACA 1428
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1728 ACTTAATTACAGCAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAG 1777
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1828 GAAGACCGCACCCNGCTGCTTTCCGGCGGA.........ACAAATTTAAA 1868
              |||:::           |||||||||         ::::::   ||
 259 ProLeuArgSer.........SerGlyGlyValPhePheAsnGlyThrAs 272

1869 CGGCAACATC.........ACGCAAACAAACGGCAAACTGTTTTTCAGCG 1909
     |||||||:::         :::  ||||||::::::::::::|||:::
 272 nGlyAsnMetValLeuAsnValGlyThrAsnSerArgValLeuPheAsnL 289

1910 GCAGACCGACACCGCACGCCTACAATCATTTAGGAAGCGGGTGGTCAAAA 1959
       :::|||:::   ::::::   |||                 ||||||
 289 euLysProAsnGluAsnThrAsnAsn.................SerLys 299

1960 ATGGAAGGTATCCCACAAGGAGAAATCGTGTGGGACAACGACTGGATCNA 2009
                                                 :::
 300 Pro.......................................LeuPr 302

2010 CCGCACGTTTAAAGCGGAAAATTTCCATATTCAGGGCGGGCAGGCGGTGA 2059
           |||:::|||:::           |||    ||||||
 302 oLeuGlnPheAsnAlaAsnIleThrAlaIleGlyGlyGly.......... 315

2060 TTTCCCGCAATGTTGCCAAAGTGGAAGGCGATTGNCATTGAGCAATCAC 2109
                       :::|||:::   |||    |||    :::||||||
 316 .................SerValSerPheAspIleHis...AlaAsnHis 325

2110 GCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCATACAATCTGTAC 2159
     :::              |||    :::    :::    :::       ::
 326 Ser............GlyArgGlyAlaGluLeuLysMetAsnThrIleAs 338

2160 ACGTTCGGACTGGACNGGTCTGACAAATTGTGTCGAANAAANCATTACCG 2209
     :    ||||||    |||:::|||||||         :::::::::   :::
 338 nIleSerAspGlyThrSerLeuThr......LeuGlnSerHisValArgL 353

2210 ACGATAAAGTGATT.................................... 2223
        |||:::::::::
 353 ysAspSerAlaPheIleIleSerLysAspLeuThrIleAsnAlaThrGly 369

2223 .................................................. 2223

 370 SerAsnPheThrLeuGluGlnSerProAspSerPheThrAspLysTyrPr 386

2224 ..........GCTTCATTGACTAAG......ACNGACNTNAGCGGCANTG 2257
                    |||    ||||||        |||    :::::::|||    |
 386 oGlyArgAlaIleSerSerThrLysAsnIleThrIleSerGlyGlyAsnV 403

2258 TNAGNCTNNCCNATNACGNTNNTTNAAANCTCNCNGGGCNTGCNNCACTN 2307
     |||:::|||                              :::::::::   :::
 403 alSerLeuGlyGlyGln..............AsnSerSerSerAspIle 414

2308 AANGGCAATCTTAGTGCAAATGGCGATACACGTTATACAGTC...AGCCA 2354
         ||||||::::::    :::::::::|||:::    |||:::    :::||
 415 LysGlyAsnIleThrIleLysSerSerThrAsnValThrLeuLysAlaHi 431

2355 CAACGCCACCCAAAAC.......................GGCAACCTTA 2380
     |||||:::   ::::::                          |||||||||:
 431 sAsnSerProArgAspPheAlaSerArgThrLeuThrLeuGlyAsnLeuA 448

2381 GCCTCGTGGGCAATGCCCAAGCAACATTTAATCAAGCCACATTAAACGGC 2430
     :::::    ||||||              |||    :::    |||    :::::::|||
 448 snValGluGlyAsnLeuThrLeuThrGlySerValAlaAspIleLysGly 464

2431 AACNCATCGGNTTCGGGCAATGCTTCATTT.................... 2460
     |||    |||         ::::::|||:::|||
 465 AsnLeuSerIleLeuAsnAspAlaThrPheLysGlyGluThrSerGluAs 481

2460 .................................................. 2460

 481 nLeuAsnIleThrGlyAsnPheThrAsnAsnGlyThrAlaAspIleAsnI 498

2461 .................AATCTAAGCAACAACGCCGCACAAAACGGCAGT 2493
                       |||:::::::::|||    :::::::::|||:::

 498 leLysGlnGlyValValAsnIleGlnGlyAsnIleThrAsnLysGlyGly 514

2494 CTGACGCTTTCCGACAACGCTAAGGCAAACGTAAGCCATTCCGCACTCAA 2543
     |||:::::::::    |||||||:::    |||    :::    :::    :::||
 515 LeuAsnIleThrThrAsnAlaGlnAsnAsn...GlnLysThrIleIleAs 530

2544 CGGCAATGTCTCCCTAGCCGATAAGGCAGTATTCCATTTGAAAACAGCC 2593
     |||||||::::::
 530 nGlyAsnIleThr..................................... 534

2594 GCTTTACCGGACAACTCAGCGGCAGCAAGGANACAGCATTACACTTAAAA 2643
                                   ::::::      |||:::::::|||
 535 ......................AsnGluGlyGlyAspLeuAsnIleLys 543

2644 GACAGCGAATGGACGCTGCCGTCAGGCACGGAATTA.........GGCAA 2684
     ||||||:::             :::::::::|||:::         |||||
 544 AspSerAsn...........AsnAsnAlaGluIleGlnIleGlyGlyAs 556

2685 TTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCACG 2734
     |::::::     ::::::::::::|||::::::|||               |
 556 nIleSerGlnLysLysGlyAsnLeuThrIleSerSer...........A 569

2735 AT.............................GCTGCAGGCGCGCAAACC 2754
     ||                                  ||||||:::::
 569 spLysIleAsnIleThrLysLysIleThrIleLysAlaGlyValAspGlu 585

2755 GGCAGNGTGTCAGACACGCCGCGCCGCCGTTCGCGCCGTTCCCTATTATC 2804
     |||        :::::::|||      :::::::::      ::::::
 586 GlyGlySerAspSerSerProAlaSerAsnAlaAsnLeuThrIle..... 600

2805 CGTTACACCGCCAACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAA 2854
                                :::    :::||||||    ::::
 601 ..........................LysThrLysThrLeuGluLeuT 608

2855 ACGGCAAATTGAACNGTCAAGGAACATTCCGCTTTATGTCGGAACTCTTC 2904
     :::|||    ||||||    :::|||       :::       :::|||:::
 608 hrGlyAspLeuAsnIleSerGlyPheAsnLys......AlaGluIleThr 622

2905 GGCTACCGAAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGNACTTA 2954
     :::    :::::::::    |||    ::::::::::::|||:::|||
 623 AlaLysAsnGlyAsnAspLeuThrIleGlyLysAlaSerAspGly..... 637

2955 CACCTTGGCGGTCAACAATACCGGCAACGAACCCGTAAGCCTCGATCAAT 3004
                       |||::::::    :::    |||::::::|||::::
 638 ................AsnAlaAsnAlaLysLysValThrPheAspLysV 649

3005 TGACGGTAGTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAAT 3054
     ::                    ||||||:::|||        :::::::::     |||
 649 al...............LysAspSerLysIleSerAlaAsnGlyHisAsn 660

3055 TTCACCCTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACT 3104
      |||
 661 ValThr............................................ 662

3105 CATCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAG 3154

 662 .................................................. 662

3155 AGCTTTCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAA 3204
       |||::::::|||:::          :::::::::    ::::::|||:::
 663 ..LeuAsnSerLysValGluThrSerAsnSerAspSerSerAlaAspAsp 678

3205 GACAACGCGCAAAGCCTTGACGCGCTGATTGCGGCCGGGCGCGATGCCGC 3254
     :::|||    ::::::                 |||:::|||    :::|||::::::
 679 SerAsnAspAsnAsnThrGlyLeuThrIleSerAla...LysAspValTh 694

3255 CGAAAAGACAGAAAGCGTTGCCGAACCGGCCCGGCNGGCAGGCGGGGAAA 3304
     :
 694 r................................................. 694

3305 ATGTCGGCATTATGCAGGCGGAGGAAGAGAAAAAACGGGTGCAGGCGGAT 3354
                                          |||:::    |||
 695 ...................................ValAsnAsnAsp 698
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 3355 AAAGACAGCGCNTTGGCGAAACAGCGCGAAGCGGAAACCCGGCCGGNTAC 3404
          |||       :::   :::   :::|||   |||         ||
  699 ValThrSerHisLysThrIleAsnIleSerAlaThrThrGlyAsnValTh 715

 3405 CACCGCCTTCCCCCGCGCCCGCNGCGCCCGCCGGGATTTGCCGCAACCGC 3454
      ||||
  715 rThr..................................................... 716

 3455 AGCCCCAACCGCAACCTCAACCCCAACCGCAGCGCGACCTGATNAGCCGT 3504

  716 ..................................................... 716

 3505 TATGCCAATAGCGGTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTTTT 3554
                          :::   |||:::|||:::||| |||
  717 .....................LysGluSerThrThrIleAsn.AlaAla. 725

 3555 CGCCGTACAGGACGAATTGGACCGCGTGTTTGCCGAAGACCGCCGCAACG 3604
                          |||:::   :::      ||||||   |||
  726 ....................ThrGlySerValGluValThrAlaLysThr 735

 3605 CNGTTTGGACAAGCNGCATCCGGNACACCAAACACTACCGTTCGCAAGAT 3654
                        |||||||||                   ||
  736 Gly.........AspIleSerGlyThr.....................Il 742

 3655 TTCCGCGCCTACCGCCAACAAACCGACCTGCGCCAAATCGGTATGCAGAA 3704
      ||||:::   |||:::|||      |||:::::::   |||:::      :
  742 eSerGlyAsnThrValAsn...ValThrAlaThrAspSerLeuThrThrG 758

 3705 AAACCTCGGCAGCGGGCGCGTCGGCATCCTGTTTTCGCACAACCGGACCG 3754
      ::               ||||||:::|||          :::::|||
  758 ln..............AlaSerSerSerIleThrSerSerAsnGlyGln 769

 3755 AAAACANCTTCGACGACGGCATCGGCAACTCGGCACGGCTTGCCCACGGC 3804
         |||   ::::::      ::::::          ::::::   :::||
  770 ThrThrLeuThrAlaLysAsnGlySerIleAlaGlySerIleAspAlaAl 786

 3805 GCCGTTTTCGGGCAATACGGCATCGGCAGGTTCGACATCGGCATCAGCAC 3854
      |      :::   ||||||:::::::::   :::|||   |||:::::::
  786 aAsnValThrLeuAsnThrThrGlyThrLeuThrThrValAlaGlySerA 803

 3855 GGGCGCGGGTTTTAGCAGCGGCANTCTNTCAGACGGCATCGGAGGCAAAA 3904
      ::   ::::::   :::::::::   :::   :::|||:::::||||||
  803 snIleLysAlaThrSerGlyThrLeuAlaIleAsnAlaLysAspAlaLys 819

 3905 TCCGCCGCCGCGTGCTGCATTACGGCATTCAGGCACGATACCGCGCCGGT 3954
            :::::::::                        |||   :::   ||
  820 LeuAspGlyThrAla..............SerGlyAspArgThrValVa 831

 3955 TTCGGCGGATTCGGCATCGAACCGTACATCGGCGCAACGCGCTATTTCGT 4004
      |:::|||   :::||||||:::      |||:::      |||   ||||
  831 lAsnAlaThrAsnAlaSerGlySerGlySerValThrAlaAlaThrSerS 848

 4005 CCAAAAAGCGGATTACCGCTACGAAAACGTCAATATCGCCACCCCCGGTC 4054
      ||:::   :::|||||||:::      ::::::|||:::
  848 erAsnValAsnIleThrGlyAspLeuSerThrIleAsnGly......... 861

 4055 TTGCGTTCAACCGNTACCGNGCGGGCATTAAGGCAGATTATTCATTCAAA 4104
                                      :::||||||   :::||
  862 ............................LeuAsnIleIleSerLysAs 868

 4105 CCGGCGCAACACA 4117
      |   :::||||||
  868 nGlyLysAsnThr 872
```

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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01827

seq_documentation_block:
ID   AAB01827 standard; Protein; 969 AA.
XX
AC   AAB01827;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain Joyc mature HMW2A protein, SEQ ID NO:32.
XX
KW   Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain Joyc.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52178.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 8; Fig 19A-O; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   969 AA;
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alignment_scores:
           Quality:  261.00              Length:   1169
             Ratio:  0.505                 Gaps:     53
 Percent Similarity:  44.226   Percent Identity: 19.247

alignment_block:
 US-09-303-518D-651 x AAB01827   ..

 Align seg 1/1  to: AAB01827  from: 1  to: 969
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1015 AACGAAAAGGTNTCCAATCCAAAGCTTAAAGTACAGACAGTCCGACTGTT 1064
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   3 AsnValSerIleGluAsnProSerThrGlu.................... 12

1065 TGACGAATCTTTGAATGAAACTGATAAAGAACCAGTTTACGCGGCAGGGG 1114
                |||::::::::::::::      |||::::::    |
  13 ..........ArgAsnAspSerAsnGluAspLeuGluTyrThrGlyThrG 26

1115 GTGTTAATCAGTACCGTCCAAGGTTAAACAACGGT............... 1149
     ||   |||        :::|||::::::||||||
  26 lyGluAsnIleAsnAsnProLysValAsnAsnGlnSerLysLysThrLeu 42

1150 ...............GAAAACCTT...........TCTTTTATCGATTA 1172
                    ||||||:::          ||||||:::::
  43 ThrSerSerIleLeuGluAsnIleLeuLysLysGlySerPheValAsnIl 59

1173 C...GGCAACGGCAAACTCATCTTATCAAACAACATCAACCAAGGC...G 1216
         ::::::   ::::::   :::::::::::||||||   |||   :
  59 eThrAlaThrAspAsnIleTyrValAsnSerSerIleAsnIleGlyAspS 76

1217 CGGGCGGTTTGTATTTGAAGGTGATTTTACGGTCTCGCCTGAAAACAAC 1266
     ::|||   |||   ::::::|||
  76 erGlyHisLeuIleLeuSerGlyGlyGlyArg.................. 86

1267 GAAACGTGGCAAGGCGCGGGCGTTCATATCAGTGAAGACAGTACCGTTAC 1316
             :::|||:::||||||   |||::::::::::   |||   ||
  87 .........AsnGlyGlyGlyValLysIleAsnLysAsnIleThrSerTh 100

1317 TTGGAAAGTAAACGGCGTGGCAAACGACCGCCTGTCCAAAATCGGCAAAG 1366
     |                                                 |
 100 r.........................................GlyG 102

1367 GCACGCTGCACGTTCAAGCCAAAGGG......GAAAACCAAGGCTCGATC 1410
     ||:::|||   :::::::::||||||       :::   :::::::::|||
 102 lySerLeuThrIleAsnSerLysGlyTrpValAspIleHisSerAsnIle 118

1411 AGCGTGGGC.......................GACGGTACAGTCATTTT 1436
     |||:::|||                       :::|||:::|||   ::
 119 SerLeuGlyThrGlyPheLeuAsnIleThrSerAsnGlySerValAlaPh 135

1437 GGATCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCG 1486
     :::::::          ||||||::::::::::   |||   :::::::|||
 135 eGluLysAlaAspLysAspLysAlaArgSerAlaAlaAspAlaGlnIle. 151

1487 GCTTGNTCAGCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTC 1536
              ::::::|||   ::::::|||:::::::::|||:::
 152 ........ValAlaGlnGlyIleIleAsnLeuThrGlyGluAsnLys... 164

1537 AACCCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAA 1586
                           ||||||   :::::::::::||||||
 165 ....................ThrPheArgLeuAsnAsnValSerLeuAs 174

1587 CGGGCATTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGA 1636
     ||||                                 :::   :::|||
 174 nGly...........................ValGlyGlnGlyLeuS 181

1637 TGATTGNCNATCATAATGCCACAACAACA...........TCCACCGTT 1674
       |||:::::::::   ::::::   |||              :::   :::
 181 erIleThrSerAsnValGlyAsnGlnThrHisLysPheAspGlyGluIle 197

1675 ACCATTACAGGGAATGAAAGTATTACACAA.................... 1704
     :::||||||||||||   :::|||:::|||
 198 AsnIleThrGlyAsnValThrIleAsnGlnThrAlaProAlaThrThrAl 214

1705 ..................CCGAGTGGTAAGAATATCAATAGACTTAATT 1735
                           |||   |||:::::   ||||||
 214 aTyrTrpAsnPheSerTyrAspSerTyrTrpAsnValSerThrLeuAsnV 231

1736 ACAGCAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACC 1785
       :::|||            |||:::   |||               |||
 231 alGlnLys...........AsnSerSerPheThrPheIleLysArgThr 243

1786 AAAACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCG 1835
```

```
     :::::|||                    :::   |||::::::     ||
 244 GluSerAsnArg...............PheGlyProThrThrProLeuAr 255

1836 CACCCNGCTGCTTTCCGGCGGA.........ACAAATTTAAACGGCAACA 1876
     |:::          |||||||||         ::::::   |||||||||:
 255 gSer.........SerGlyGlyValPhePheAsnGlyThrAsnGlyAsnM 269

1877 TC.........ACGCAAACAAACGGCAAACTGTTTTTCAGCGGCAGACCG 1917
     ::           :::   |||||:::::::::::::|||:::   :::|||
 269 etValLeuAsnValGlyThrAsnSerArgValLeuPheAsnLeuLysPro 285

1918 ACACCGCACGCCTACAATCATTTAGGAAGCGGGTGGTCAAAAATGGAAGG 1967
     :::   ::::::   |||                   ||||||
 286 AsnGluAsnThrAsnAsn..................SerLysPro..... 294

1968 TATCCCACAAGGAGAAATCGTGTGGGACAACGACTGGATCNACCGCACGT 2017
                                         :::         |
 295 ...................................LeuProLeuGlnP 299

2018 TTAAAGCGGAAAATTTCCATATTCAGGGCGGGCAGGCGGTGATTTCCCGC 2067
     ||:::|||:::          |||   ||||||
 299 heAsnAlaAsnIleThrAlaIleGlyGlyGly.................. 309

2068 AATGTTGCCAAAGTGGAAGGCGATTGNCATTTGAGCAATCACGCCCAAGC 2117
             :::|||:::   |||   |||   :::||||||:::
 310 .........SerValSerPheAspIleHis...AlaAsnHisSer..... 320

2118 AGTTTTTGGTGTCGCACCGCATCAAAGCCATACAATCTGTACACGTTCGG 2167
            |||   :::   :::   :::   :::      :::   ||||
 321 .......GlyArgGlyAlaGluLeuLysMetAsnThrIleAsnIleSerA 335

2168 ACTGGACNGGTCTGACAAATTGTGTCGAANAAANCATTACCGACGATAAA 2217
     ||   |||:::||||||        :::::::::   :::      |||:::
 335 spGlyThrSerLeuThr......LeuGlnSerHisValArgLysAspSer 349

2218 GTGATT............................................ 2223
     ::::::
 350 AlaPheIleIleSerLysAspLeuThrIleAsnAlaThrGlySerAsnPh 366

2223 .................................................. 2223

 366 eThrLeuGluGlnSerProAspSerPheThrAspLysTyrProGlyArgA 383

2224 ..GCTTCATTGACTAAG......ACNGACNTNAGCGGCANTGTNAGNCTN 2265
        |||   ||||||       |||   :::::::|||   |||:::|||
 383 laIleSerSerThrLysAsnIleThrIleSerGlyGlyAsnValSerLeu 399

2266 NCCNATNACGNTNNTTNAAANCTCNCNGGGCNTGCNNCACTNAANGGCAA 2315
                                ::::::::   :::   |||||
 400 GlyGlyGln...............AsnSerSerSerAspIleLysGlyAs 411

2316 TCTTAGTGCAAATGGCGATACACGTTATACAGTC...AGCCACAACGCCA 2362
     |:::::   :::::::::|||:::   |||:::   :::||||||:::
 411 nIleThrIleLysSerSerThrAsnValThrLeuLysAlaHisAsnSerP 428

2363 CCCAAAAC.......................GGCAACCTTAGCCTCGTG 2388
       ::::::                         |||||||||::::::
 428 roArgAspPheAlaSerArgThrLeuThrLeuGlyAsnLeuAsnValGlu 444

2389 GGCAATGCCCAAGCAACATTTAATCAAGCCACATTAAACGGCAACNCATC 2438
     ||||||         |||   :::   |||   ::::::||||||   ||
 445 GlyAsnLeuThrLeuThrGlySerValAlaAspIleLysGlyAsnLeuSe 461

2439 GGNTTCGGGCAATGCTTCATTT........................... 2460
     |     ::::::|||:::|||
 461 rIleLeuAsnAspAlaThrPheLysGlyGluThrSerGluAsnLeuAsnI 478

2460 .................................................. 2460

 478 leThrGlyAsnPheThrAsnAsnGlyThrAlaAspIleAsnIleLysGln 494

2461 .........AATCTAAGCAACAACGCCGCACAAAACGGCAGTCTGACGCT 2501
             |||::::::::|||   :::::::::|||:::|||:::::
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 495 GlyValValAsnIleGlnGlyAsnIleThrAsnLysGlyGlyLeuAsnIl 511

2502 TTCCGACAACGCTAAGGCAAACGTAAGCCATTCCGCACTCAACGGCAATG 2551
     ::::   ||||||:::   |||   :::   :::   :::||||||||||:
 511 eThrThrAsnAlaGlnAsnAsn...GlnLysThrIleIleAsnGlyAsnI 527

2552 TCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAACAGCCGCTTTACC 2601
     :::::
 527 leThr..................................................... 528

2602 GGACAACTCAGCGGCAGCAAGGANACAGCATTACACTTAAAAGACAGCGA 2651
                  ::::::         |||::::::||||||||::
 529 ..............AsnGluGlyGlyAspLeuAsnIleLysAspSerAs 540

2652 ATGGACGCTGCCGTCAGGCACGGAATTA.........GGCAATTTAAACC 2692
     :            :::::::::|||:::         ||||||::::::
 540 n............AsnAsnAlaGluIleGlnIleGlyGlyAsnIleSerG 553

2693 TTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGAT...... 2736
          ::::::::::::|||::::::|||            |||
 553 lnLysLysGlyAsnLeuThrIleSerSer............AspLysIle 565

2737 .......................GCTGCAGGCGCGCAAACCGGCAGNGT 2762
                              ||||||:::::   |||
 566 AsnIleThrLysLysIleThrIleLysAlaGlyValAspGluGlyGlySe 582

2763 GTCAGACACGCCGCGCCGCCGTTCGCGCCGTTCCCTATTATCCGTTACAC 2812
      :::::::::|||      :::::::::   ::::::
 582 rAspSerSerProAlaSerAsnAlaAsnLeuThrIle.............. 594

2813 CGCCAACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAA 2862
                       :::   :::|||||||   :::::::|||
 595 ....................LysThrLysThrLeuGluLeuThrGlyAsp 604

2863 TTGAACNGTCAAGGAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCG 2912
     ||||||   :::|||      :::      :::|||:::   :::   ::
 605 LeuAsnIleSerGlyPheAsnLys......AlaGluIleThrAlaLysAs 619

2913 AAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGNACTTACACCTTGG 2962
     :::::::   |||   :::::::::::::|||:::|||
 619 nGlyAsnAspLeuThrIleGlyLysAlaSerAspGly.............. 631

2963 CGGTCAACAATACCGGCAACGAACCCGTAAGCCTCGATCAATTGACGGTA 3012
               |||::::::   :::   |||::::::|||::::::
 632 ........AsnAlaAsnAlaLysLysValThrPheAspLysVal...... 643

3013 GTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCACCCT 3062
               ||||||:::|||      :::::::::   |||   |||
 644 .........LysAspSerLysIleSerAlaAsnGlyHisAsnValThr.. 656

3063 GCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACTCATCCGCA 3112

 656 ..................................................... 656

3113 AAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCC 3162
                                                  |||:::
 657 ..............................................LeuAsn 658

3163 GACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGC 3212
     :::|||:::     :::::::::   ::::::|||:::   :::|||
 659 SerLysValGluThrSerAsnSerAspSerSerAlaAspAspSerAsnAs 675

3213 GCAAAGCCTTGACGCGCTGATTGCGGCCGGGCGCGATGCCGCCGAAAAGA 3262
      ::::::          |||:::|||   :::|||::::::
 675 pAsnAsnThrGlyLeuThrIleSerAla...LysAspValThr....... 688

3263 CAGAAAGCGTTGCCGAACCGGCCCGGCNGGCAGGCGGGGAAAATGTCGGC 3312

 688 ..................................................... 688

3313 ATTATGCAGGCGGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACAG 3362
                                 |||:::   |||      ||
 689 ............................ValAsnAsnAspValThrSe 695
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3363 CGCNTTGGCGAAACAGCGCGAAGCGGAAACCCGGCCGGNTACCACCGCCT 3412
     |      :::   :::   :::|||   |||         ||||||
 695 rHisLysThrIleAsnIleSerAlaThrThrGlyAsnValThrThr.... 710

3413 TCCCCCGCGCCCGCNGCGCCCGCCGGGATTTGCCGCAACCGCAGCCCCAA 3462

 710 ..................................................... 710

3463 CCGCAACCTCAACCCCAACCGCAGCGCGACCTGATNAGCCGTTATGCCAA 3512

 710 ..................................................... 710

3513 TAGCGGTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTTTTCGCCGTAC 3562
                  :::   |||:::|||:::||| |||
 711 ............LysGluSerThrThrIleAsn.AlaAla......... 719

3563 AGGACGAATTGGACCGCGTGTTTGCCGAAGACCGCCGCAACGCNGTTTGG 3612
                  |||:::   :::       ||||||   |||
 720 ............ThrGlySerValGluValThrAlaLysThrGly..... 730

3613 ACAAGCNGCATCCGGNACACCAAACACTACCGTTCGCAAGATTTCCGCGC 3662
               |||||||||                        ||||||:::
 731 ....AspIleSerGlyThr.....................IleSerGlyA 739

3663 CTACCGCCAACAAACCGACCTGCGCCAAATCGGTATGCAGAAAAACCTCG 3712
       |||:::|||      |||::::::   |||:::      :::
 739 snThrValAsn...ValThrAlaThrAspSerLeuThrThrGln...... 752

3713 GCAGCGGGCGCGTCGGCATCCTGTTTTCGCACAACCGGACCGAAAACANC 3762
               ||||||:::|||         ::::::|||      |||
 753 .........AlaSerSerSerIleThrSerSerAsnGlyGlnThrThrLe 766

3763 TTCGACGACGGCATCGGCAACTCGGCACGGCTTGCCCACGGCGCCGTTTT 3812
      ::::::      ::::::         ::::::   :::|||      :
 766 uThrAlaLysAsnGlySerIleAlaGlySerIleAspAlaAlaAsnValT 783

3813 CGGGCAATACGGCATCGGCAGGTTCGACATCGGCATCAGCACGGGCGCGG 3862
     ::   |||||:::::::::   :::|||   |||:::::::::   :::
 783 hrLeuAsnThrThrGlyThrLeuThrThrValAlaGlySerAsnIleLys 799

3863 GTTTTAGCAGCGGCANTCTNTCAGACGGCATCGGAGGCAAAATCCGCCGC 3912
     :::   :::::::::   :::   :::|||::::::|||||      ::
 800 AlaThrSerGlyThrLeuAlaIleAsnAlaLysAspAlaLysLeuAspGl 816

3913 CGCGTGCTGCATTACGGCATTCAGGCACGATACCGCGCCGGTTTCGGCGG 3962
     :::::::                  |||   :::   |||:::|||
 816 yThrAla..............SerGlyAspArgThrValValAsnAlaT 828

3963 ATTCGGCATCGAACCGTACATCGGCGCAACGCGCTATTTCGTCCAAAAAG 4012
       :::||||||:::      |||:::      |||   ||||||:::
 828 hrAsnAlaSerGlySerGlySerValThrAlaAlaThrSerSerAsnVal 844

4013 CGGATTACCGCTACGAAAACGTCAATATCGCCACCCCCGGTCTTGCGTTC 4062
     :::|||||||:::      ::::::|||:::
 845 AsnIleThrGlyAspLeuSerThrIleAsnGly..................  855

4063 AACCGNTACCGNGCGGGCATTAAGGCAGATTATTCATTCAAACCGGCGCA 4112
                                 :::||||||   :::|||   :::|
 856 .....................LeuAsnIleIleSerLysAsnGlyLysA 865

4113 ACACA 4117
     |||||
 865 snThr 866
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:AAU37120

seq_documentation_block:
ID AAU37120 standard; Protein; 2344 AA.
XX
AC AAU37120;
XX
DT 14-FEB-2002 (first entry)

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XX
DE   Staphylococcus aureus cellular proliferation protein #1290.
XX
KW   Antisense; prokaryotic cellular proliferation protein;
KW   antibiotic; antibacterial; drug design.
XX
OS   Staphylococcus aureus.
XX
PN   WO200170955-A2.
XX
PD   27-SEP-2001.
XX
PF   21-MAR-2001; 2001WO-US09180.
XX
PR   21-MAR-2000; 2000US-191078P.
PR   23-MAY-2000; 2000US-206848P.
PR   26-MAY-2000; 2000US-207727P.
PR   23-OCT-2000; 2000US-242578P.
PR   27-NOV-2000; 2000US-253625P.
PR   22-DEC-2000; 2000US-257931P.
PR   16-FEB-2001; 2001US-269308P.
XX
PA   (ELIT-) ELITRA PHARM INC.
XX
PI   Haselbeck R,  Ohlsen KL,  Zyskind JW,  Wall D,  Trawick JD,  Carr GJ;
PI   Yamamoto RT,  Xu HH;
XX
DR   WPI; 2001-611495/70.
DR   N-PSDB; AAS54979.
XX
PT   New polynucleotides for the identification and development of
PT   antibiotics, comprise sequences of antisense nucleic acids -
XX
PS   Example 3; Seq ID No 12713; 511pp; English.
XX
CC   The invention relates to antisense inhibitors of genes essential to
CC   prokaryotic cellular proliferation, their use in identifying the
CC   genes, their use in the discovery of novel antibiotics, the essential
CC   genes themselves and the encoded proteins. The prokaryotes used are
CC   Escherichia coli, Staphylococcus aureus, Salmonella typhi, Klebsiella
CC   pneumoniae, Pseudomonas aeruginosa and Enterococcus faecalis. The
CC   invention is also useful for the identification of potential new targets
CC   for antibiotic development. The antisense nucleic acids can also be used
CC   to identify proteins used in proliferation, to express these proteins,
CC   and to obtain antibodies capable of binding to the expressed proteins.
CC   The proteins can be used to screen compounds in rational drug discovery
CC   programmes. The antisense nucleic acid sequence is also useful to screen
CC   for homologous nucleic acids which are required for cell proliferation in
CC   a wide variety of organisms. The present sequence represents an
CC   essential prokaryotic cellular proliferation protein.
CC   Note: The sequence data for this patent did not form part
CC   of the printed specification, but was obtained in electronic
CC   format directly from WIPO at
CC   ftp.wipo.int/pub/published_pct_sequences.
XX
SQ   Sequence   2344 AA;


alignment_scores:
            Quality:  260.00              Length:   1577
              Ratio:  0.344                 Gaps:     59
 Percent Similarity:  47.876   Percent Identity: 18.199

alignment_block:
 US-09-303-518D-651 x AAU37120   ..

 Align seg 1/1  to: AAU37120  from: 1  to: 2344

     163 CGCGACTTTGCCGAAAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATAT 212
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      20 ArgLeuTyrLysSerGlyLysAsnTrpValLysSerGlyIleLysGluIl 36

     213 TGAGGTNTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAG 262
         ||||::::::::      |||
      36 eGluMetPheLysIleMetGly.........................L 44

     263 CCCCGATGATTGATTTTTCTGTGGTGTCGCGTAACGGC..... 300
           |||:::|||:::   |||:::||||||:::::::::
      44 euProPheIleSerHisSerMetValSerGlnAspAsnGlnSerIleSer 60

     301 ..........................GTGGCGGCATTGGTGGGCGATCA 323
                                    ::::::|||::::::|||
      61 LysLysMetThrGlyTyrGlyLeuLysThrThrAlaValIleGlyGlyAl 77

     324 ATATATTGTGAGCGTGGCACATAAC..... 348
          :::   |||::::::   |||:::
      77 aPheThrValAsnMetLeuHisAspGlnGlnAlaPheAlaAlaSerAspA 94

     349 .....................................GGCGGCTAT 357
                                             |||:::
      94 laProLeuThrSerGluLeuAsnThrGlnSerGluThrValGlyAsnGln 110

     358 AACAACGTTGATTTTGGTGCGGAAGGAAGNAATCCCGATCAGCACCGTTT 407
         |||::::::   :::   |||:::   ::::::   |||:::
     111 AsnSerThrThrIleAspAlaSerThrSerThrAlaAspSer........ 124

     408 TTCTTACCAAATTGTGAAAAGAAATAATTATAAGCCTGACAATTCACACC 457
                       |||   :::|||:::   :::   ::::::|||
     125 .......ThrSerValThrLysAsnSerSerSerValGlnThrSer.... 137

     458 CTTACAACGGCGATTANCATATGCCGCGTTTGCATAAATTTGTCACAGAT 507
               |||:::|||:::          :::      :::   |||||||:::
     138 .....AsnSerAspThrValSerSerGluLysSerGluAsnValThrSer 152

     508 ....................................GCAGAACCTGTCGA 521
                                            ::::::      ||
     153 ThrThrAsnSerThrSerAsnGlnGlnGluLysLeuThrSerThrSerGl 169

     522 AATGACGAGTGACATGAGGGGGAATACCTATTCCGATAAAGAAAAATATC 571
         |   ||||||:::   :::   ::::::   ||||||    |||:::::::
     169 uSerThrSerSerLysAsnThrThrSerSerSerAsp.ThrLysSerVal 185

     572 CCGAGCGTGTCCGCATCGGCTCAGGACACCACTATTGGCGTTATGATGAT 621
            |||:::|||::::::   |||      :::   ::::::   :::
     186 ThrSerThrSerSerThrGluGlnProIleAsnThrSerThrAsnGlnSe 202

     622 GACA.........AACACGGCGATTTATCCTACTCCGGCGCATGGTTAAT 662
          |||          ||||||:::          ||||||:::   :::   |
     202 rThrAlaSerAsnAsnThrSerGlnSerThrThrProThrSerAlaAsnL 219

     663 TG............................GCGGCAATACACATATGC 682
         ||                           |||   :::   :::
     219 euAsnLysThrSerThrThrSerThrSerThrAlaProValLysLeu... 234

     683 AGGGTTGGGGAAATAATGGCGTANTTAGTTTGAGCGGCGATGTGCGCCAT 732
                   :::   ::::::   |||:::   ::::::::::::::
     235 .........ArgThrPheSerArgLeuAlaMetSerThrPheAlaSerAl 248

     733 GCCAACGACTATGGCCCTATGCCGATTGCAGGTGCGG..... 769
               ||||||   ||||||          :::
     248 aAlaThrThrThrAlaLeuThrAlaAsnThrIleThrValAsnLysAspA 265

     770 .........................................CAGGCG 775
                                                 |||:::
     265 snLeuLysGlnTyrMetThrThrSerGlyAsnAlaThrTyrAspGlnSer 281

     776 ACAGCGGTTCGCCAATGTTTATTTATGACAAAACAAACAATAAATGGCTG 825
         |||  |||          ::       |||   |||:::::::|||
     282 Thr..GlyValValThrLeuThrGlnAspThrThrSerGlnLysGlyAla 297

     826 CTC.........................................AACGG 833
         :::                                         :::||
     298 IleThrLeuGlyThrArgIleAspSerAsnLysSerPheHisPheSerGl 314

     834 AGTTTTACAAACCGGCTACCCTTATTCCGGCAGGGAAAACGGTTTCCAGC 883
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 314 yLysValAsnLeuGlyAsnLysTyrGluGlyHisGlyAsnGly..... 328

 884 TGATACGCAAAGATTGGTTCTACGATGACATTTACAGAGGCGATACACAT 933
                                          ||||||
 329 .....GlyAspGlyIle 332

 934 ACCGTCTNTTTTGAACCGCGCAGTAACGGACATTTTTCCTTTACATCCAA 983
          :::|||::|||         |||:::   ::::::::::::
 333 GlyPheAlaPheSerProGlyValLeuGlyGluThrGlyLeuAsnGlyAl 349

 984 C.....AACAACGGTACGGGTACGGTAACAGAAA 1012
                          :::|||:::   |||         :::|
 349 aAlaValGlyIleGlyGlyLeuSerAsnAlaPheGlyPheLysLeuAspT 366

1013 CCAACGAAAAGGTNTCCAATCCAAAGCTTAAAGTACAGACAGTCCGACTG 1062
     ||   :::::::::|||:::|||
 366 hrTyrHisAsnThrSerThrPro..... 373

1063 TTTGACGAATCTTTGAATGAAACTGATAAAGAACCAGTTTACGCGGCAGG 1112
          :::|||     ::::::      :::|||      :::|||||
 374 ......AsnSerSerAlaLysAlaLysAlaAspProSerAsnValAlaGl 388

1113 GGGTGTTAATCAGTACCGTCCAAGGTTAAACAACGGTGAAAACCTTTCTT 1162
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 388 yGly.....GlyAlaPheGlyAlaP 395

1163 TTATC.....GATTACGGCAACGGCAAACTCATCTTATCAAACAAC 1203
     ||:::         :::||||||   ::::::          |||::::::
 395 heValThrThrAspSerTyrGlyValAlaSerThrTyrThrSerSerSer 411

1204 ATCAACCAAGGCGCGGGCGGTTTGTATTTTGAAGGTGATTTTACGGTCTC 1253
          ::::::|||:::   |||                  :::|||::
 412 ThrAlaAspAsnAlaAlaLysLeu.....AsnValGl 422

1254 GCCTGAAAACAACGAAACGTGGCAAGGCGCGGGCGTTCATATCAGTGAAG 1303
     :|||   ||||||   |||:::|||         ::::::   :::   |
 422 nProThrAsnAsn...ThrPheGlnAspPheAspIleAsnTyrAsnGlyA 438

1304 ACAGTACCGTT.....ACTTGGAAAGTAAAC 1329
     ||:::   |||                |||||      |||
 438 spThrLysValMetThrValLysTyrAlaGlyGlnThrTrpThrArgAsn 454

1330 GGCGTGGCAAACGACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACGT 1379
          :::|||   ::::::|||   |||      ::::::   ::
 455 ......IleSerAspTrpIleAlaLysSerGlyThrThrAsnPheSerLe 469

1380 TCAAGCCAAAGGGGAAAACCAAGGCTCGATCAGC.....GTGGGCG 1420
     ::::      :::::::::   |||:::   :::         |||
 469 uSerMetThrAlaSerThrGlyGlyAlaThrAsnLeuGlnGlnValGlnP 486

1421 ACGGTACAGTCATTTTGGATCAGCAGGCAGACGATAAAGGCAAAAAACAA 1470
       ||||||          ::::::|||      :::   :::
 486 heGlyThrPheGluTyrThrGluSerAlaValThrGlnValArg..... 500

1471 GCCTTTAGTGAAATCGGCTTGNTCAGCGGCAGG..... 1503
               :::   :::::::::|||:::
 501 .....TyrValAspValThrThrGlyLysAspIleIleProProLy 514

1504 .....GGTACGGTGCAA.....CTGAATGCCGATAATCAG.... 1533
               |||:::|||:::      ::::::   |||||||||
 514 sThrTyrSerGlyAsnValAspGlnValValThrIleAspAsnGlnGlnS 531

1534 .....TTCAACCCCGACAAACTCTATTTCGGCTTT 1563
                    ::::|||      ::::::      ::::::
 531 erAlaLeuThrAlaLysGlyTyrAsnTyrThrSerValAspSerSerTyr 547

1564 CGCGGCGGACGTTTGGATTTAAAC.....GG 1589
     :::         |||   |||                          ||
 548 AlaSerThrTyrAsnAspThrAsnLysThrValLysMetThrAsnAlaGl 564

1590 GCATTCGCTTTCGTTCCACCGTATT.....1614
     |:::|||:::::::::::
 564 yGlnSerValThrTyrTyrPheThrAspValLysAlaProThrValThrV 581

1615 .....CAAAATACCGATGAAGGG.....GCGATG 1638
               |||:::   :::   |||                ::::::
 581 alGlyAsnGlnThrIleGluValGlyLysThrMetAsnProIleValLeu 597

1639 ATTGNCNATCATAATGCCACAACAACATCCACCGTTACCATTACAGGGAA 1688
        ::::::   |||:::|||   |||   |||   |||:::||||||
 598 ThrThrThrAspAsnGlyThrGlyThrValThrAsnThrValThrGly.. 613

1689 TGAAAGTATTACACAACCGAGTGGTAAGAATATCAATAGACTTAATTACA 1738
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 614 .....LeuProSerGly.....LeuSerTyr. 620

1739 GCAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAA..... 1776
          :::   |||   |||:::   :::|||
 621 .....AspSerAlaThrAsnSerIleIleGlyThrProThrLysIleGly 635

1777 .....GATACGACCAAAACGAACGGGCGG..... 1800
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 636 GlnSerThrValThrValValSerThrAspGlnAlaAsnAsnLysSerTh 652

1801 .....CTCAACCTTGTT.....TACCAGC 1819
                    :::|||:::|||                |
 652 rThrThrPheThrIleAsnValValAspThrThrAlaProThrValThrP 669

1820 CCGCCGCAGAAGACCGCACCCNGCTGCTTTCCGGCGGAACAAATTTAAAC 1869
     ||   ::::::      :::   :::::::|||      :::   :::|||
 669 roIleGlyAspLysSerSerGluValPheSerProIleSerProIleAsn 685

1870 GGCAACATCACGCAAACAAACGGCAAACTGTTTTTCAGCGGCAGACCGAC 1919
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 686 ...IleAlaThrGlnAspAsn.....SerGlyAsnAlaVa 696

1920 ACCGCACGCCTACAATCATTTAGGAAGCGGGTGGTCAAAAATGGAAGGTA 1969
     :   ::::::                                  :::   |||:
 696 lThrAsnThr.....ValThrGlyL 703

1970 TCCCACAAGGAGAAATCGTGTGGGACAACGACTGGATCNACCGCACGTTT 2019
     ::|||:::|||                                  ||||||
 703 euProSerGly.....LeuThrPhe 709

2020 AAAGCGGAAAATTTCCATATTCAGGGCGGGCAGGCGGTGATTTCCCGCAA 2069
        ::   |||      |||:::|||      :::   |||:::   ::
 710 AspSerThrAsnAsnThrIleSerGlyThrProThrAsnIleGlyThrSe 726

2070 TGTTGCCAAAGTGGAAGGCGATTGNCATTTGAGCAATCACGCCCAAGCAG 2119
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 726 rThrIleThrIleValSerThrAspAlaSerGlyAsnLysThrThrThrT 743

2120 TTTTTGGT.....GTCGCACCGCATCAAAGCCATACAATCTGTACA 2160
     ::|||          :::      :::|||   ::::::   |||
 743 hrPheLysTyrGluValThrArgAsnSerMetSerAspSerValSerThr 759

2161 CGTTCGGACTGGACNGGTCTGACAAATTGTGTCGAANAAANCATTACCGA 2210
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 760 .....SerGlySerThrGln...GlnSerGlnSerValSerTh 771

2211 CGATAAAGTGATTGCTTCATTGACTAAGACNGACNTNAGCGGCANTGTNA 2260
     :::|||:::   ::::::   :::::::|||:::::::||||||::::::
 771 rSerLysAlaAspSerGlnSerAlaSerThrSerThrSerGlySerIleM 788

2261 GNCTNNCCNATNACGNTNNTTNAAANCTCNCNGGGCNTGCNNCACTNAAN 2310
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 788 etThrSerThrSerAlaSerThrSerLysSerThrSerValSerLeuSer 804

2311 GGCAATCTTAGTGCAAATGGCGATACACGTTATACAGTCAGCCACAACGC 2360
        ::::::||||||:::   :::         :::   |||::::::::
 805 AspSerValSerAlaSerLysSerLeuSerThrSerGluSerAsnSerVa 821

2361 CACCCAAAACGGCAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATTTA 2410
     ::::::::::   :::   |||||||||   |||:::|||::::::
 821 lSerSerSerThrSerThrSerLeuVal...AsnSerGlnSerVal.... 835
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     1424 rThrSerSerTyrThrSerGlnSer.........ThrSerGlnSerGluS 1438

     4017 TTACCGCTACGAAAACGTCAATATCGCCACCCCCGGTCTTGCGTTCAACC 4066
          |||:::|||:::|||||||:::|||                  ||||||
     1438 erThrSerThrSerThrSerLeuSerAsp..............SerThr 1449

     4067 GNTACCGNGCGGGCATTAAGGCAG 4090
          :::   :::::::::      |||
     1450 SerIleSerLysSerThrSerGln 1457

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seq_documentation_block:
ID   AAR41724 standard; Protein; 1477 AA.
XX
AC   AAR41724;
XX
DT   26-APR-1994  (first entry)
XX
DE   High molecular weight protein 2 (HMW2).
XX
KW   HMW; high molecular weight protein; virus; vaccine; influenza;
KW   epitope; immunity; haemophilus influenzae.
XX
OS   Haemophilus influenzae.
XX
PN   WO9319090-A.
XX
PD   30-SEP-1993.
XX
PF   16-MAR-1993;   93WO-US02166.
XX
PR   16-MAR-1992;   92GB-0005704.
XX
PA   (BARE/) BARENKAMP S J.
PA   (INRM ) INSERM INST NAT SANTE & RECH  MEDICALE.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1993-320683/40.
DR   N-PSDB; AAQ49507.
XX
PT   High molecular weight surface proteins - of non-typeable
PT   haemophilus which exhibit immunogenic properties .
XX
PS   Claim 4; Figure 4; 100pp; English.
XX
CC   The isolation and purification of the high molecular weight protein
CC   enables the identification of the major protective epitopes of the
CC   protein by conventional epitope mapping.  These epitopes can then be
CC   synthesised using standard techniques and incorporated into fully
CC   synthetic or recombinant vaccines.
XX
SQ   Sequence   1477 AA;


alignment_scores:
           Quality:  259.50            Length:   1395
             Ratio:  0.425               Gaps:     63
 Percent Similarity:  43.728   Percent Identity: 19.068

alignment_block:
 US-09-303-518D-651 x AAR41724   ..

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     178 AATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTNTACAACAA 227
         |||:::||||||:::::::::         |||            :::||
     282 AsnGlnGlyLysLeuSerAla.........AspSerValSerLysAspLy 295

     228 AAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGATT 277
         |:::|||:::::|||   ::::::                     |||
     295 sSerGlyAsnIleValLeuSerAlaLysGluGlyGluAlaGluIleGlyG 312

     278 TTTCTGTGGTGTCGCGTAAC..............GGCGTGGCGGCATTG 312
               :::   :::::|||                |||        :::
     312 lyValIleSerAlaGlnAsnGlnAlaLysGlyGlyLysLeuMetIle 328

     313 GTGGGCGATCAATATATTGTGAGCGTG.....................GC 341
         :::||||||:::      :::::::::                     ::
     329 ThrGlyAspLysValThrLeuLysThrGlyAlaValIleAspLeuSerGl 345

     342 ACATAACGGCGGC......TATAACAACGTTGATTTTGGTGCGGAAGGAA 385
         :   :::||||||      |||   :::   |||      :::||||||
     345 yLysGluGlyGlyGluThrTyrLeuGlyGlyAspGluArgGlyGluGlyL 362

     386 GNAATCCCGATCAGCACCGTTTTTCTTACCAAATTGTGAAAAGAAATAAT 435
           |||                 :::   |||::::::|||:::
     362 ysAsn.................GlyIleGlnLeuAlaLysLys...... 370

     436 TATAAGCCTGACAATTCACACCCTTACAACGGCGATTANCATATGCCGCG 485

     370 ..................................................  370

     486 TTTGCATAAATTTGTCACAGATGCAGAACCTGTCGAAATGACGAGTGACA 535
                                                   ||||||
     371 ..........................................ThrSerLeuG 374

     536 TGAGGGGGAATACC......TATTCCGATAAAGAAAAATATCCCGAGCGT 579
           :::|||:::|||         |||   |||||||||
     374 luLysGlySerThrIleAsnValSerGlyLysGluLys............ 386

     580 GTCCGCATCGGCTCAGGACACCACTATTGGCGTTATGATGATGACAAACA 629
                 |||:::            |||
     387 .........GlyGlyArgAlaIleValTrp..................... 393

     630 CGGCGATTTATCCTACTCCGGCGCATGGTTAATTGGCGGCAATACACATA 679
          ||||||::::::                ||||||   ||||||   :::
     394 .GlyAspIleAla..............LeuIleAspGlyAsnIleAsnA 405

     680 TGCAGGGTTGGGGAAATAATGGCGTANTTAGTTTGAGCGGCGATGTGCGC 729
           ||||||                          ||||||||||:::
     405 laGlnGly.........................SerGlyAspIleAla 412

     730 CATGCCAACGACTATGGCCCTATGCCGATTGCAGGTGCGGCAGGCGACAG 779
           :::                          ::::||   :::      ||
     413 LysThr.....................GlyGlyPheValGluThrSe 421

     780 CGGTTCGCCAATGTTTATTTATGACAAAACAAACAATAAATGGCTGCTCA 829
         ||||      :::||||||   |||                      |
     421 rGlyHisAspLeuPheIleLysAsp.....................A 430

     830 ACGGAGTTTTACAAACCGGCTACCCTTATTCCGGCAGGGAAAACGGTTTC 879
         ||:::::::::::::::
     430 snAlaIleValAspAla............................... 435

     880 CAGCTGATACGCAAAGATTGGTTCTACGAT..................... 909
                 |||:::|||:::   |||
     436 ............LysGluTrpLeuLeuAspPheAspAsnValSerIleAs 448

     910 .......GACATTTACAGAGGCGATACACATACCGTCTNTTTTGAACCGC 952
               |||      |||::::::|||                  |||
     448 nAlaGluAspProLeuArgAsnAsnThrGlyIleAsnAspGluPheProT 465

     953 GCAGTAACGGACATTTTTCCTTTACATCCAACAACAACGGTACGGGTACG 1002
           ::::::|||:::   |||      ::::::|||:::         |||
     465 hrGlyThrGlyGluAlaSerAspProLysLysAsnSerGluLeuLysThr 481

    1003 GTAACAGAAACCAACGAAAAGGTNTCCAATCCAAAGCTTAAAGTACAGAC 1052
           |||   ||||||      :::||||||         ::::::   ||
     482 ...ThrLeuThrAsnThrThrIleSerAsnTyrLeuLysAsnAlaTrpTh 497

    1053 AGTCCGACTGTTTGACGAATCTTTGAATGAAACTGATAAAGAACCAGTTT 1102
         |:::               :::::::::   :::   |||      |||
     497 rMet..............AsnIleThrAlaSerArgLysLeuThrValA 509
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 952 .....ThrThr 953

2773 CCGCGCCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTC 2822
          :::|||::::::||||||:::::::::
 954 HisAlaLysArgAsnGlnArgSerIleIleGly..... 964

2823 GGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACNGTC 2872
                    :::   ::::::   :::|||:::||||||
 965 .............GlyAspIleIleAsnLysLysGlySerLeuAsnIleT 977

2873 AAGGAACATTCCGCTTTATGTCG...GAACTCTTCGGCTACCGAAGCGAC 2919
       :::   :::      :::   ::::::   |||      |||:::
 977 hrAspSerAsnAsnAspAlaGluIleGlnIleGlyGlyAsnIleSerGln 993

2920 AAATTGAAGCTGGCGGAAAGTTCCGAAGGNACTTACACCTTGGCG..... 2964
     |||                        |||||||:::   |||::::::
 994 Lys.....................GluGlyAsnLeuThrIleSerSerAs 1003

2965 ....GTCAACAATACCGGCAACGAACCCGTAAGCCTCGATCAATTGACGG 3010
         :::|||   |||                          |||:::|||:
1003 pLysIleAsnIleThr.....................LysGlnIleThrI 1013

3011 TAGTGGAAGGGAAAGACAACAAACCGCTGTCC............GAAAAC 3048
     ::   :::|||   |||::::::      |||            :::|||
1013 leLysLysGlyIleAspGlyGluAspSerSerSerAspAlaThrSerAsn 1029

3049 CTTAATTTCACCCTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTA 3098
        |||:::|||::::::
1030 AlaAsnLeuThrIleLys.............................. 1035

3099 CCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAG 3148
                                                :::|||||
1036 .....ThrLysG 1038

3149 AACAAGAGCTTTCCGACAAACTC.............GGCAAGGCAGAA 3183
     ||   :::|||::::::   |||              :::|||||||||
1038 luLeuLysLeuThrGluAspLeuSerIleSerGlyPheAsnLysAlaGlu 1054

3184 GCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTGACGCGCTGAT 3233
                  :::   ||||||
1055 Ile.........ThrAlaLysAsp..................... 1059

3234 TGCGGCCGGGCGCGATGCCGCCGAAAAGACAGAAAGCGTTGCCGAACCGG 3283
           |||||||||
1060 .......GlyArgAspLeu.......................... 1063

3284 CCCGGCNGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCGGAGGAAGAG 3333
        :::   |||::::::|||   |||          ||||||   :::
1064 .....ThrIleGlyAsnSerAsnAspGlyAsnSerGlyAlaGluAlaLys 1078

3334 AAAAAACGGGTGCAGGCGGATAAAGACAGCGCNTTGGCGAAACAGCGCGA 3383
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3384 AGCGGAAACC.........CGGCCGGNTACCACCGCCTTCCCCCGCGCCC 3424
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1095 sAsnValThrLeuAsnSerLysValLysThrSerSerSerAsnGlyGlyA 1112

3425 GCNGCGCCCGCCGGGATTTGCCGCAACCGCAGCCCCAACCGCAACCTCAA 3474
     ||   ::::::   |||                                :::
1112 rgGluSerAsnSerAspAsnAspThrGlyLeuThrIleThrAlaLysAsn 1128

3475 CCCCAACCGCAGCGCGACCTGATNAGC...CGTTATGCCAATAGCGGTTT 3521
        :::   ::::::|||:::::::|||   :::   :::|||
1129 ValGluValAsnLysAspIleThrSerLeuLysThrValAsnIleThrAl 1145

3522 GAGTGAATTTTCCGCCACGCTCAACAGCGTTTTCGCCGTACAGGACGAAT 3571
      ||||||      :::||| :::::::::   :::          ||||||
1145 aSerGluLysValThrThr.ThrAlaGlySerThrIleAsnAlaThrAsn 1161

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           |||   :::          ::::::          |||      ::
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3622 ATCCGGNACACCAAACACTACCGTTCGC...AAGATTTCCGCGCCTACCG 3668
     ::::::::|||   ::::::::::::          :::::::::   ::::
1178 rGlyAsnThrValSerValSerAlaThrValAspLeuThrThrLysSerG 1195

3669 CCAACAAACCGACCTGCGCCAAATCGGTATGCAGAAAAACCTCGGCAGCG 3718
     :::::|||      :::   ::::::   ::::::   ||||||||:::
1195 lySerLysIleGluAlaLysSerGlyGluAlaAsnValThrSerAlaThr 1211

3719 GGCGCGTCGGCATCCTGTTTTCGCACAACCGGACCGAAAACANCTTCGAC 3768
     |||:::   ::::::         |||   :::   :::|||   :::::
1212 GlyThrIleGlyGly.........ThrIleSerGlyAsnThrValAsnVa 1225

3769 GACGGCATCGGCA.................................A 3782
     :||||||:::|||                                :
1225 lThrAlaAsnAlaGlyAspLeuThrValGlyAsnGlyAlaGluIleAsnA 1242

3783 CTCGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAAT......ACGGCA 3826
     ::   :::|||      |||          :::||||||      |||:::
1242 laThrGluGlyAlaAlaThrLeuThrAlaThrGlyAsnThrLeuThrThr 1258

3827 TCGGCAGGTTCGACATCGGCATCAGCACGGGCGCGGGTTTTAGCAGCGGC 3876
     :::|||||||||:::   :::|||:::::::::::::|||         ||
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3877 ANTCTNTCAGACGGCATCGGAGGCAAAATCCGCCGCCGCGTGCTGCATTA 3926
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1275 a......GlnAsnGlySerIleAlaGlySerIleAsnAlaAlaAsnValT 1290

3927 CGGCATTCAGGCACGATACCGCGCCGGTTTCGGCGGATTCGGCATCGAAC 3976
     ||               |||      :::   |||   |||      :::
1290 hrLeuAsnThrThrGlyThrLeuThrThrValAlaGlySerAspIleLys 1306

3977 CGTACATCGGCGCAACGCGCTATTTCGTCCAAA 4009
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1307 AlaThrSerGlyThrLeuValIleAsnAlaLys 1317
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1993.DAT:AAR41732

seq_documentation_block:

ID AAR41732 standard; Protein; 1529 AA.
XX
AC AAR41732;
XX
DT 26-APR-1994 (first entry)
XX
DE High molecular weight protein 4 (HMW4).
XX
KW HMW; high molecular weight protein; virus; vaccine; influenza;
KW epitope; immunity; haemophilus influenzae.
XX
OS Haemophilus influenzae.
XX
PN WO9319090-A.
XX
PD 30-SEP-1993.
XX
PF 16-MAR-1993; 93WO-US02166.
XX
PR 16-MAR-1992; 92GB-0005704.
XX
PA (BARE/) BARENKAMP S J.
PA (INRM) INSERM INST NAT SANTE & RECH MEDICALE.
XX
PI Barenkamp SJ;
XX
DR WPI; 1993-320683/40.
DR N-PSDB; AAQ49511.
XX
PT High molecular weight surface proteins - of non-typeable
PT haemophilus which exhibit immunogenic properties
XX
PS Claim 6; Figure 10; 100pp; English.

XX
CC The isolation and purification of the high molecular weight protein
CC enables the identification of the major protective epitopes of the
CC protein by conventional epitope mapping. These epitopes can then be
CC synthesised using standard techniques and incorporated into fully
CC synthetic or recombinant vaccines.
XX
SQ Sequence 1529 AA;

alignment_scores:
Quality: 258.00 Length: 1121
Ratio: 0.484 Gaps: 51
Percent Similarity: 47.547 Percent Identity: 20.428

alignment_block:
US-09-303-518D-651 x AAR41732 ..

Align seq 1/1 to: AAR41732 from: 1 to: 1529

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616 LeuArgSerSerArgArgSerPheAlaGlyValHis.PheAsnGlyIleG 632

149 ACTACCAATACTATCGCGACTTTGCCGAAAATAAAGGCAAGTTTGCAGTC 198
632 ly.........................GlyLysThrAsnPheAsnIle 639

199 GGGGCGAAAGATATTGAGGTNTACAACAAAAAAGGGGAGTTGGTCGGCAA 248
640 GlyAlaAsnAlaLysAlaLeuPheLysLeuLysProAsnAlaAlaThrAs 656

249 ATCAATGACAAAAGCCCCGATGATTGATTTTTCTGTGGTGTCGCGTAACG 298
656 pProLysLysGluLeuProIle.....ThrPheAsnAlaAsnI 669

299 GCGTGGCGGCATTGGTGGGCGATCAATATATTGTGAGCGTGGCACATAAC 348
669 leThrAlaThrGlyAsnSerAspSerSerValMetPheAspIleHis... 684

349 GGCGGCTATAACAACGTTGATTTTGGTGCGGAAGGAAGNAATCCCGATCA 398
685 .........AlaAsnLeuThrSerArgAlaAlaGlyIleAsnMetAspSe 698

399 GCACCGTTTTTCT.....TACCAAATTGTGAAAAGAAATAATT 436
698 rIleAsnIleThrGlyGlyLeuAspPheSerIleThrSerHisAsnArg. 714

437 ATAAGCCTGACAATTCACACCCTTACAACGGCGATTANCATATGCCGCGT 486
715 ...........AsnSerAsnAlaPhe.....Glu 720

487 TTGCATAAATTTGTCACAGATGCAGAACCTGTCGAAATGACGAGTGACAT 536
721 IleLysLys.....AspLeuThrIleAsnAl 729

537 GAGGGGGAATACCTATTCCGATAAAGAAAAATATCCCGAGCGTGTCCGCA 586
729 aThrGlySerAsnPheSerLeuLysGlnThr..... 739

587 TCGGCTCAGGACACCACTATTGGCGTTATGATGATGACAAACACGGCGAT 636
740 .....LysAspSerPheTyrAsnGluTyr......SerLysHisAlaIle 752

637 TTATCCTACTCCGGCGCATGGTTAATTGGCGGCAATACACATATGCAGGG 686
753 AsnSerSerHisAsnLeuThrIleLeuGlyGlyAsnValThrLeu..... 767

687 TTGGGGAAATAATGGCGTANTTAGTTTGAGCGGCGATGTGCGCCATGCCA 736
768 .GlyGlyGluAsnSerSerSerSerIleThrGlyAsnIleAsnIleThrA 784

737 ACGACTATGGCCCTATGCCGATTGCAGGTGCGGCAGGCGACAGCGGTTCG 786

784 snLysAlaAsn.....ValThrLeuGlnAlaAspThrSerAsnSer 797

787 CCAATGTTTATTTATGACAAAACA.....AACAATAAATGGCTGCT 827
798 AsnThrGlyLeuLysLysArgThrLeuThrLeuGlyAsnIleSerValGl 814

828 CAACGGAGTTTTACAAACCGGCTACCCTTATTCCGGCAGGGAAAACGGTT 877
814 uGlyAsnLeuSerLeuThrGly.....AlaAsnAlaA 825

878 TCCAGCTGATACGCAAAGATTGGTTCTACGATGACATTTACAGAGGCGAT 927
825 snIleValGlyAsnLeuSerIleAlaGluAspSerThrPheLysGlyGlu 841

928 ACACATACCGTCTNTTTTGAACCGCGCAGTAACGGACATTTTTCCTTTAC 977
842 Ala.....Se 843

978 ATCCAACAACAACGGTACGGGTACGGTAACAGAAACCAACGAAAAGGTNT 1027
843 rAspAsnLeuAsnIleThrGlyThrPhe.....ThrAsnAsnGlyThrA 858

1028 CCAATCCAAAGCTTAAAGTACAGACAGTCCGACTGTTTGACGAATCTTTG 1077
858 laAsnIleAsnIleLysGlnGlyValValLysLeuGlnGlyAspIleIle 874

1078 AATGAAACTGATAAAGAACCAGTTTACGCGGCAGGGGGTGTTAATCAGTA 1127
875 AsnLys.....GlyGly..... 878

1128 CCGTCCAAGGTTAAACAACGGTGAAAACCTTTCTTTTATCGATTACGGCA 1177
879 .....LeuAsnIleThrThrAsnAlaSer.....GlyT 888

1178 ACGGCAAACTCATCTTATCAAACAACATCAACCAAGGCGCGGGCGGTTTG 1227
888 hrGlnLysThrIleIleAsnGlyAsnIleThrAsnGluLysGlyAspLeu 904

1228 TATTTT..... 1233
905 AsnIleLysAsnIleLysAlaAspAlaGluIleGlnIleGlyGlyAsnIl 921

1234 .....GAAGGTGATTTTACGGTCTCGCCTGAAAACAACGAAACGT 1273
921 eSerGlnLysGluGlyAsnLeuThrIleSerSerAspLys..... 934

1274 GGCAAGGCGCGGGCGTTCATATCAGTGAAGACAGTACCGTTACTTGGAAA 1323
935 .....ValAsnIleThrAsnGlnIleThrIleLysAlaGly 946

1324 GTAAACGGCGTGGCAAACGACCGCCTGTCCAAAATCGGCAAAGGCACGCT 1373
947 ValGluGlyGlyArgSerAspSer...SerGluAlaGluAsnAlaAsnLe 962

1374 GCACGTTCAAGCCAAA.....G 1390
962 uThrIleGlnThrLysGluLeuLysLeuAlaGlyAspLeuAsnIleSerG 979

1391 GGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGAT 1440
979 lyPheAsnLysAlaGluIleThrAlaLysAsnGlySerAspLeu..... 993

1441 CAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTT 1490
994 .....ThrIleGlyAs 997

1491 GNTCAGCGGCAGGGGTACGGTGCAACTGAATGCCGAT...AATCAGTTCA 1537
997 nAlaSerGlyGly.....AsnAlaAspAlaLysLysValT 1009

1538 ACCCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAAC 1587
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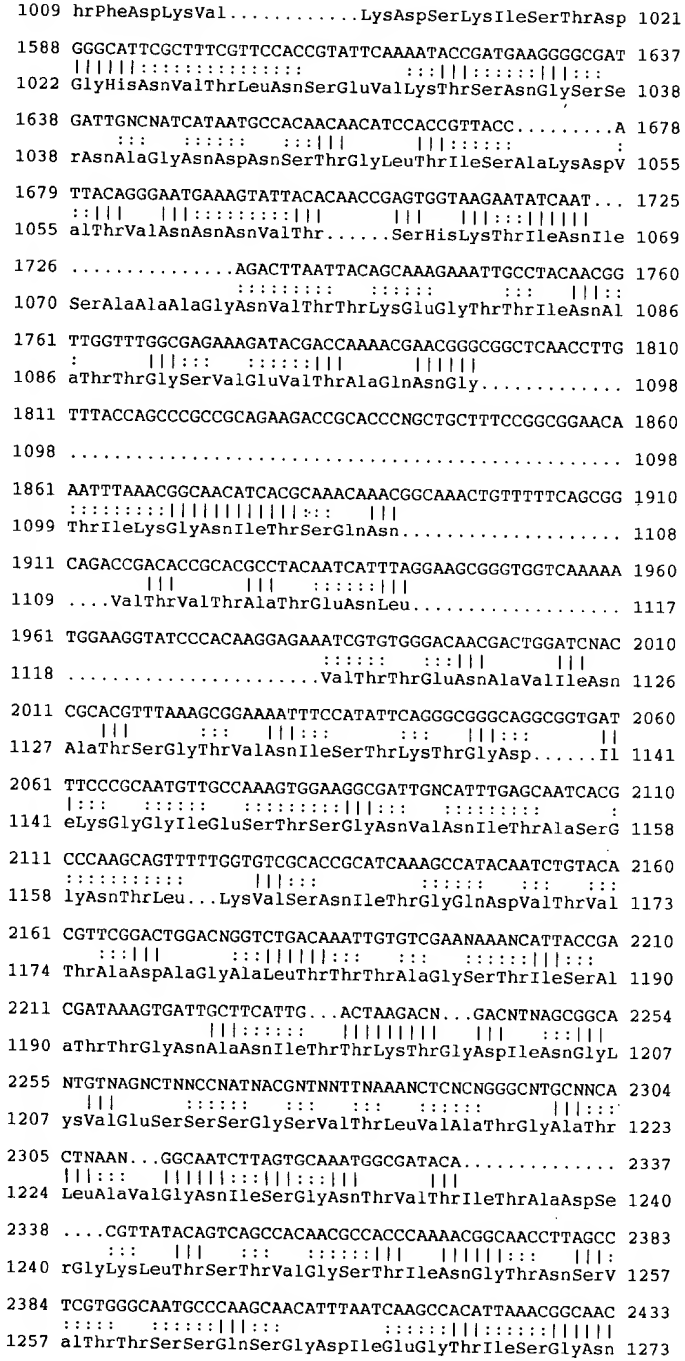
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1638 GATTGNCNATCATAATGCCACAACAACATCCACCGTTACC.....A 1678
1038 rAsnAlaGlyAsnAspAsnSerThrGlyLeuThrIleSerAlaLysAspV 1055
1679 TTACAGGGAATGAAAGTATTACACAACCGAGTGGTAAGAATATCAAT... 1725
1055 alThrValAsnAsnAsnValThr.....SerHisLysThrIleAsnIle 1069
1726 .....AGACTTAATTACAGCAAAGAAATTGCCTACAACGG 1760
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1761 TTGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGCGGCTCAACCTTG 1810
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1861 AATTTAAACGGCAACATCACGCAAACAAACGGCAAACTGTTTTTCAGCGG 1910
1099 ThrIleLysGlyAsnIleThrSerGlnAsn..... 1108
1911 CAGACCGACACCGCACGCCTACAATCATTTAGGAAGCGGGTGGTCAAAAA 1960
1109 ....ValThrValThrAlaThrGluAsnLeu..... 1117
1961 TGGAAGGTATCCCACAAGGAGAAATCGTGTGGGACAACGACTGGATCNAC 2010
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2255 NTGTNAGNCTNNCCNATNACGNTNNTTNAAANCTCNCNGGGCNTGCNNCA 2304
1207 ysValGluSerSerSerGlySerValThrLeuValAlaThrGlyAlaThr 1223
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1224 LeuAlaValGlyAsnIleSerGlyAsnThrValThrIleThrAlaAspSe 1240
2338 ....CGTTATACAGTCAGCCACAACGCCACCCAAAACGGCAACCTTAGCC 2383
1240 rGlyLysLeuThrSerThrValGlySerThrIleAsnGlyThrAsnSerV 1257
2384 TCGTGGGCAATGCCCAAGCAACATTTAATCAAGCCACATTAAACGGCAAC 2433
1257 alThrThrSerSerGlnSerGlyAspIleGluGlyThrIleSerGlyAsn 1273
2434 NCATCGGNTTCGGGCAATGCTTCATTTAATCTAAGCAACAACGCCGCACA 2483
1274 Thr.....ValAsnValThrAlaSe 1280
2484 AAACGGCAGTCTGACGCTTTCCGACAACGCTAAGGCAAACGTAAGCCATT 2533
1280 rThrGlyAspLeuThrIleGlyAsnSerAlaLysValGluAlaLysAsnG 1297
2534 CCGCACTCAACGGCAATGTCTCCCTAGCCGATAAGGCAGTATTCCATTTT 2583
1297 lyAla.....AlaThrLeuThrAla 1303
2584 GAAAACAGCCGCTTTACCGGACAA.....CTCAGCGGCAG 2618
1304 GluSerGlyLysLeuThrThrGlnThrGlySerSerIleThrSerSerAs 1320
2619 CAAGGANACAGCATTACACTTAAAAGACAGCGAATGGACGCTGCCGTCAG 2668
1320 nGlyGlnThrThrLeuThrAlaLysAspSer..... 1330
2669 GCACGGAATTAGGCAATTTAAACCTTGACAACGCCACCATTACACTCAAT 2718
1331 ..SerIleAlaGlyAsnIleAsnAla.....AlaAsnValThrLeuAsn 1344
2719 TCCGCCTATCGCCACGATGCTGCAGGCGCGCAAACCGGCAGNGTGTCAGA 2768
1345 Thr.....ThrGlyThr..... 1348
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1349 .....LeuThrThrThrGlyAspS 1355
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1355 erLysIleAsnAlaThrSerGlyThrLeuThrIleAsnAlaLys..... 1369
2869 NGTCAAGGAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGAAGCGA 2918
1370 .....AspAl 1371
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1371 aLysLeuAspGlyAlaAlaSerGlyAspArgThrValValAsnAlaThrA 1388
2969 ACAATACCGGCAACGAACCCGTAAGCCTCGATCAATTGACGGTAGTGGAA 3018
1388 snAlaSerGlySerGlyAsnValThrAlaLysThrSerSerValAsn 1404
3019 GGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAA 3068
1405 IleThrGlyAspLeuAsnThrIleAsnGlyLeuAsnIleIleSerGluAs 1421
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1421 n.....GlyArgAsnThrValArgLeuArgGlyLysGluI 1433
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XX
AC   AAY81609;
XX
DT   24-MAY-2000  (first entry)
XX
DE   Streptococcus pneumoniae type 4 protein sequence #109.
XX
KW   Streptococcus pneumoniae; vaccine; screening; protein antigen;
KW   antibacterial; antiinflammatory; meningitis; infection; diagnosis;
KW   pneumococcal disease.
XX
OS   Streptococcus pneumoniae.
XX
PN   WO200006737-A2.
XX
PD   10-FEB-2000.
XX
PF   27-JUL-1999;   99WO-GB02451.
XX
PR   27-JUL-1998;   98GB-0016337.
PR   19-MAR-1999;   99US-0125164.
XX
PA   (MICR-) MICROBIAL TECHNICS LTD.
XX
PI   Gilbert CFG,  Hansbro PM;
XX
DR   WPI; 2000-195300/17.
XX
PT   New Streptococcal protein, useful as a vaccine, for diagnosis of
PT   pneumococcal diseases and for screening agents capable of antagonizing
PT   or inhibiting expression of the protein  -
XX
PS   Claim 1; Page 83; 108pp; English.
XX
CC   AAY81501 to AAY81679 represent specifically claimed protein sequences
CC   isolated from Streptococcus pneumoniae. AAA05407 to AAA05590 represent
CC   specifically claimed nucleotide sequences isolated from S. pneumoniae.
CC   The sequences have antibacterial and antiinflammatory properties.
CC   The protein sequences, and fragments of them, are useful as immunogens
CC   and/or antigens. The nucleotide sequences can be used in vaccines and in
CC   diagnostic assays. The proteins and nucleotides can be useful for the
CC   detection and diagnosis of S. pneumoniae. The protein sequences are also
CC   useful for screening an agent capable of antagonising, inhibiting or
CC   interfering with the function or expression of the proteins in which the
CC   agent is useful for treatment or prophylaxis of S. pneumoniae infection
CC   and meningitis. AAA05591 to AAA05614 represent primers used in the
CC   exemplification of the present invention.
XX
SQ   Sequence   1237 AA;


alignment_scores:
            Quality:  257.50            Length:   1198
              Ratio:  0.441               Gaps:     43
 Percent Similarity:  48.748   Percent Identity: 19.699

alignment_block:
 US-09-303-518D-651 x AAY81609   ..

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      40 PheThrAsnGluSerAlaValLeuGluLysThrValGluLysThrAspAl 56

    1138 TTAAACAACGGTGAAAACCTTTCTTTTATCGATTACGGCAACGGCAAACT 1187
         :   :::|||      |||   :::|||:::      :::|||:::||||
      56 aLeuAlaThrAsnAspThrValValLeuGlyThrIleSerThrSerAsnS 73

    1188 CATCTTATCAAACAACA.....................TCAACCAAGGCG 1216
         ||:::   :::|||:::                      ||||||:::|||
      73 erAlaSerSerThrSerLeuSerAlaSerGluSerAlaSerThrSerAla 89

    1217 CGGGCGGTTTGTATTTTGAAGGTGATTTTACGGTCTCGCCTGAAAACAAC 1266
               :::      ::::::         :::      ::::::::
      90 SerGluSerAlaSerThrSerAlaSerThrSerAlaSerThrSerAlaSe 106

    1267 GAAACGTGGCAAGGCGCGGGCGTTCATATCAGTGAAG...ACAGTACCGT 1313
         ::::   :::::::::   |||      |||::::::   :::      :
     106 rGluSerAlaSerThrSerAlaSerThrSerIleSerAlaSerSerThrV 123

    1314 TACTTGGAAAGTAAACGGCGTGGCAAACGACCGCCTGTCCAAAATCGGCA 1363
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     123 alValGlySerGlnThrAlaAlaAlaThrGluAlaThrAlaLysLysVal 139

    1364 AAGGCACGCTGCACGTTCAAGCCAAAGGGGAAAACCAAGGCTCGATCAGC 1413
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     140 Glu...GluAspArgLysLysProAlaSerAspTyrValAlaSerValTh 155

    1414 GTGGGCGACGGTACAGTCATTTTGGATCAGCAGGCAGACGATAAAGGCAA 1463
         :   :::::::::|||||:::         |||:::            :
     155 rAsnValAsnLeuGlnSerTyrAlaLysArgArgLysArgSerValAspS 172

    1464 AAAACAAGCCTTTAGTGAAATCGGCTTGNTCAGCGGCAGGGGTACGGTGC 1513
         ::   :::   |||:::   |||      :::||||||
     172 erIleGluGlnLeuLeuAlaSerIleLysAsnAlaAlaValPheSerGly 188

    1514 AACTGAATGCCGATAATCAGTTCAACCCCGACAAACTCTATTTCGGC... 1560
         |||         |||:::::::::::::|||:::   :::   |||
     189 Asn......ThrIleValAsnGlyAlaProAlaIleAsnAlaSerLeuAs 203

    1561 .........................TTTCGCGGCGGACGTTTGGATTTAA 1585
                                   :::   |||      :::|||
     203 nIleAlaLysSerGluThrLysValTyrThrGlyGluGlyValAspSerV 220

    1586 ACGGGCATTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCG 1635
           :::         ::::::::::::::   |||::::::|||:::
     220 alTyrArgValProIleTyrTyrLysLeuLysValThrAsnAspGlySer 236

    1636 ATGATT.......................................... 1641
         :::
     237 LysLeuThrPheThrTyrThrValThrTyrValAsnProLysThrAsnAs 253

    1642 ................................GNCNATCATAATGCCA 1657
                                        :::   :::|||:::
     253 pLeuGlyAsnIleSerSerMetArgProGlyTyrSerIleTyrAsnSerG 270

    1658 CAACAACATCCACCGTTACCATTACAGGGAATGAAAGTATTACACAACCG 1707
           |||::::::   :::   :::|||   ::::::::::::   :::|||
     270 lyThrSerThrGlnThrMetLeuThrLeuGlySerAspLeuGlyLysPro 286

    1708 AGTGGTAAGAATATCAATAGACTTAATTACAGCAAAGAAATTGCCTACAA 1757
         ||||||   :::            ||||||
     287 SerGlyValLys............AsnTyr..................... 292

    1758 CGGTTGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGCGGCTCAACC 1807
                                     |||      |||||||||      |
     293 .....................IleThrAspLysAsnGlyArgGlnValL 302

    1808 TTGTTTACCAGCCCGCCGCAGAAGACCGCACCCNGCTGCTTTCCGGCGGA 1857
         ||   |||:::   :::            |||         :::|||:::
     302 euSerTyrAsnThrSer............ThrMetThrThrGlnGlySer 314

    1858 ACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACTGTTTTTCAG 1907
                  ||||||   :::|||   ||||||      |||||||::
     315 GlyTyrThrTrpGlyAsnGlyAlaGlnMetAsnGly......PhePheAl 329

    1908 CGGCAGACCGACACCGCACGCCTACAATCATTTAGGAAGCGGGTGGTCAA 1957
         :   :::            :::|||:::   |||   |||:::|||:::
     329 aLysLys............GlyTyrGly...LeuThrSerSerTrpThr. 340

    1958 AAATGGAAGGTATCCCA...CAAGGAGAAATCGTGTGGGACAACGACTGG 2004
```

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3581 TGTTTGCCGAAGACCG.....................CCGCAACGCNGTT 3609
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3610 TG..................GACAAGCNGCAT..............CCG 3626
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 951 euValHisGlnLeuGlnHisGlnArgValHisArgLeuArgArgGlnPro 967

3627 GNACACCAAACA.....................CTACCGTTCGCAAGATT 3655
       ||||||:::                    ||||||      :::
 968 ValHisGlnSerGlnGlnValProValArgGlnLeuProHisGlnGlnVa 984

3656 TCCGCGC.................................CTACCGC 3669
     ||||||                                 |||   |
 984 lProArgLeuGlnGlnAlaProValArgArgLeuGlnGlnValLeuAlaP 1001

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3720 GCGCGTCGGCATCCT.....................GTTTTCGCACA 3745
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1018 LeuAsnArgHisGlnArgValArgProLeuGlnGlnValLeuAlaProGl 1034

3746 ACCGGACCGAAAACANCTTCGACGACGGCATCGGCAACTCGGCACGGCTT 3795
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1034 nProGlnArgGlnGlnValHisArgLeuGlnArgGln..... 1046

3796 GCCCACGGCGCCGTTTTCGGGCAATACGGCATCGGCAGGTTCGA..... 3839
               |||   |||      ||||||::::::||||||
1047 ...........ArgValArgLeuAsnArgHisGlnArgValArgProLeu 1059

3840 .................................CATCGGCATCA 3850
                                      ||||||   ||
1060 GlnGlnValLeuAlaProGlnProGlnArgGlnGlnValHisArgLeuGl 1076

3851 GCACGGGCGCGGG..................................... 3863
     ||||   |||
1076 nHisGlnArgValArgProLeuGlnGlnValLeuAlaProGlnProGlnA 1093

3864 ..................TTTTAGCAGCGGCANTCTNTCAGACGGCAT 3893
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1093 rgGlnGlnValHisArgLeuGlnArgGlnArgValArgLeuSerGlnHis 1109

3894 CGGAGGCAAAATCCGCCGCCGCGTGCTGCATTACGGCATTCAGGCACGAT 3943
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1110 GlnArgValArgGlnProGlnGlnAla..................... 1118

3944 ACCGCGCCGGTTTCGGCGGATTCGGCATCGAACCGTACATCGGCGCAACG 3993
                           |||:::   ::::::   ::::::
1119 .......................HisGlnLeuLeuAsnLeuHisGlnP 1127

3994 CGCTATTTCGTCCAAAA...................AGCGGATTACCG 4022
       :::   :::|||:::                  :::   :::|||
1127 roValArgGlnProGlnHisArgGlnAlaProGlnLeuGlnGlnValPro 1143

4023 CTACGAAAACGTCAATATCGCCACCCCCGGTCTTGCGTTCAA 4064
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1144 ValArgGlnProGlnArgArgGlnValArgArgLeuGlnGln 1157
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seq_documentation_block:

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ID   AAW30292 standard; Protein; 1601 AA.
XX
AC   AAW30292;
XX
DT   14-APR-1998  (first entry)
XX
DE   Non-typeable Haemophilus high mol.wt. surface protein HMW4.
XX
KW   Non-typeable Haemophilus; high molecular weight surface protein;
KW   HMW4; immunogen; vaccine; otitis media.
XX
OS   Haemophilus influenzae strain 5.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 372
FT                   /note= "encoded by TCT"
FT   Misc-difference 400
FT                   /note= "encoded by AAT"
XX
PN   WO9736914-A1.
XX
PD   09-OCT-1997.
XX
PF   01-APR-1997;   97WO-US04707.
XX
PR   01-APR-1996;   96US-0617697.
XX
PA   (BARE/) BARENKAMP S J.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1997-503038/46.
DR   N-PSDB; AAT90993.
XX
PT   High molecular weight proteins of non-typeable Haemophilus
PT   influenzae - useful for vaccine production
XX
PS   Claim 1; Page 97-102; 183pp; English.
XX
CC   This protein comprises the high molecular weight surface protein
CC   HMW4 (123 kDa) of non-typeable Haemophilus influenzae strain 5 that
CC   has the immunological ability to protect against disease caused by
CC   a non-typeable Haemophilus strain and is characterised by at least
CC   one surface-exposed B-cell epitope that is recognised by monoclonal
CC   antibody AD6.  The HMW4 amino acid sequence was deduced from an
CC   isolated hmw4 gene (see AAT90993).  HMW1 (see AAW30293), HMW2 (see
CC   AAW30294) and HMW3 (see AAW30291) have also been identified.  A
CC   conjugate comprising HMW4 linked to an antigen, hapten or
CC   polysaccharide, and a synthetic peptide of 6-150 amino acids
CC   corresponding to at least protective epitope of HMW4 are also
CC   claimed.  HMW proteins, conjugates and peptides can be used in
CC   vaccines, as immunogens for preparation of antibodies and as
CC   antigens for detection of these antibodies.
XX
SQ   Sequence   1601 AA;
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alignment_scores:

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           Quality:  256.50              Length:   1481
             Ratio:  0.374                 Gaps:     73
 Percent Similarity:  46.253   Percent Identity: 20.257
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alignment_block:

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     158 LysAspAlaIleIleAsnThrAsnGlyPheThrAlaSerThrLeuAspIl 174

     213 TGAGGTNTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAA. 261
         |:::      |||   |||::::::          ::::::||||||
     174 eSerAsnGluAsnIleLysAlaArgAsnPheThrLeuGluGlnThrLysA 191

     262 ...........GCCCCGATGATTGATTTTTCTGTG......GTGTCGCGT 294
                 |||   :::::::::   ::::::      |||::::::
     191 spLysAlaLeuAlaGluIleValAsnHisGlyLeuIleThrValGlyLys 207

     295 AACGGCGTGGCGGCATTGGTGGGC............GATCAATATATTGT 332
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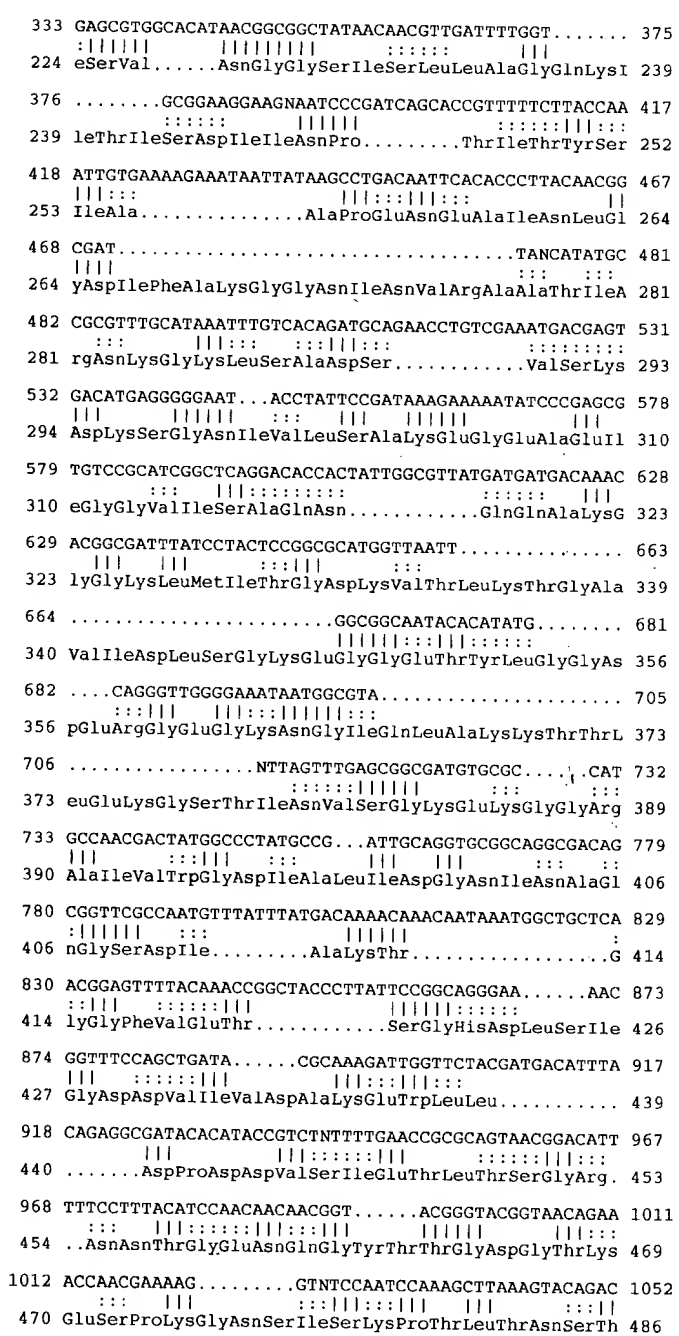

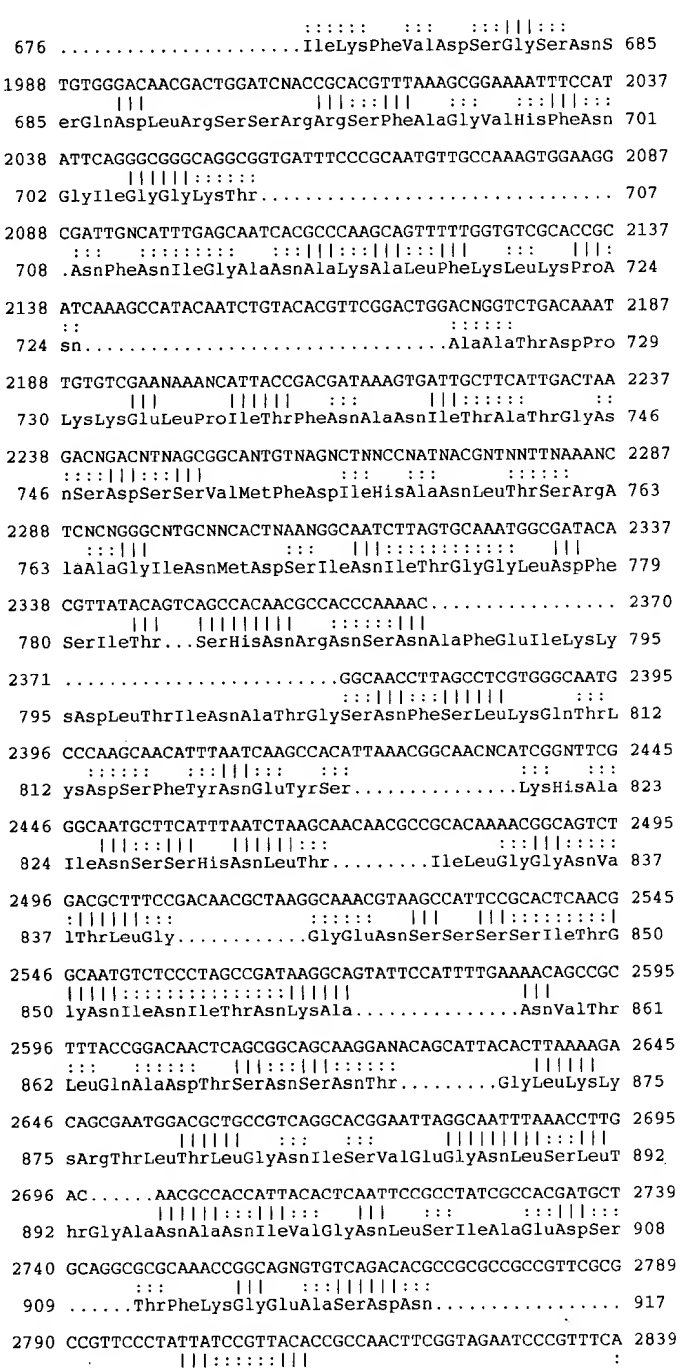
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685 erGlnAspLeuArgSerSerArgArgSerPheAlaGlyValHisPheAsn 701
2038 ATTCAGGGCGGGCAGGCGGTGATTTCCCGCAATGTTGCCAAAGTGGAAGG 2087
702 GlyIleGlyGlyLysThr..... 707
2088 CGATTGNCATTTGAGCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGC 2137
708 .AsnPheAsnIleGlyAlaAsnAlaLysAlaLeuPheLysLeuLysProA 724
2138 ATCAAAGCCATACAATCTGTACACGTTCGGACTGGACNGGTCTGACAAAT 2187
724 sn.....AlaAlaThrAspPro 729
2188 TGTGTCGAANAAANCATTACCGACGATAAAGTGATTGCTTCATTGACTAA 2237
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2238 GACNGACNTNAGCGGCANTGTNAGNCTNNCCNATNACGNTNNTTNAAANC 2287
746 nSerAspSerSerValMetPheAspIleHisAlaAsnLeuThrSerArgA 763
2288 TCNCNGGGCNTGCNNCACTNAANGGCAATCTTAGTGCAAATGGCGATACA 2337
763 laAlaGlyIleAsnMetAspSerIleAsnIleThrGlyGlyLeuAspPhe 779
2338 CGTTATACAGTCAGCCACAACGCCACCCAAAAC..... 2370
780 SerIleThr...SerHisAsnArgAsnSerAsnAlaPheGluIleLysLy 795
2371 .....GGCAACCTTAGCCTCGTGGGCAATG 2395
795 sAspLeuThrIleAsnAlaThrGlySerAsnPheSerLeuLysGlnThrL 812
2396 CCCAAGCAACATTTAATCAAGCCACATTAAACGGCAACNCATCGGNTTCG 2445
812 ysAspSerPheTyrAsnGluTyrSer.....LysHisAla 823
2446 GGCAATGCTTCATTTAATCTAAGCAACAACGCCGCACAAAACGGCAGTCT 2495
824 IleAsnSerSerHisAsnLeuThr.....IleLeuGlyGlyAsnVa 837
2496 GACGCTTTCCGACAACGCTAAGGCAAACGTAAGCCATTCCGCACTCAACG 2545
837 lThrLeuGly.....GlyGluAsnSerSerSerSerIleThrG 850
2546 GCAATGTCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAACAGCCGC 2595
850 lyAsnIleAsnIleThrAsnLysAla.....AsnValThr 861
2596 TTTACCGGACAACTCAGCGGCAGCAAGGANACAGCATTACACTTAAAAGA 2645
862 LeuGlnAlaAspThrSerAsnSerAsnThr.....GlyLeuLysLy 875
2646 CAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTG 2695
875 sArgThrLeuThrLeuGlyAsnIleSerValGluGlyAsnLeuSerLeuT 892
2696 AC.....AACGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCT 2739
892 hrGlyAlaAsnAlaAsnIleValGlyAsnLeuSerIleAlaGluAspSer 908
2740 GCAGGCGCGCAAACCGGCAGNGTGTCAGACACGCCGCGCCGCCGTTCGCG 2789
909 .....ThrPheLysGlyGluAlaSerAspAsn..... 917
2790 CCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAATCCCGTTTCA 2839


918 .....LeuAsnIleThr.....G 922
2840 ACACGCTGACGGTAAACGGCAAATTGAAC.....NGTCAAGGAACA 2880
922 lyThrPheThrAsnAsnGlyThrAlaAsnIleAsnIleLysGlnGlyVal 938
2881 TTCCGCTTTATGTCGGAACTCTTCGGCTACCGAAGCGACAAATTGAAGCT 2930
939 ValLysLeuGlnGlyAspIleIle.....AsnLysGlyGlyLeuAsnIl 953
2931 GGCGGAAAGTTCCGAAGGNACTTACACCTTGGCGGTCAACAATACC.... 2976
953 eThrThrAsnAlaSerGlyThrGlnLysThrIleIleAsnGlyAsnIleT 970
2976 2976
970 hrAsnGluLysGlyAspLeuAsnIleLysAsnIleLysAlaAspAlaGlu 986
2977 .....GGCAACGAACCCGTAAG 2993
987 IleGlnIleGlyGlyAsnIleSerGlnLysGluGlyAsnLeuThrIleSe 1003
2994 CCTCGATCAATTGACGGTAGTGGAA..... 3018
1003 rSerAspLysValAsnIleThrAsnGlnIleThrIleLysAlaGlyValG 1020
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3064 CAAAACGAACACGTCGAT.....GCCGGCGCGTG 3092
1037 GlnThrLysGluLeuLysLeuAlaGlyAspLeuAsnIleSerGlyPheAs 1053
3093 GCGTTACCAACTCATCCGCAAAGACGGC...GAGTTCCGCCTGCATAATC 3139
1053 nLysAlaGluIleThrAlaLysAsnGlySerAspLeuThrIleGlyAsnA 1070
3140 CGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAGAAGCCAAA 3189
1070 la.....SerGlyGlyAsnAlaAspAlaLys 1078
3190 AAA.....CAGGCGGAAAAAGACAACGCGCAAAGCCTTGACGCGCT 3230
1079 LysValThrPheAspLysValLysAspSerLysIleSerThrAsp..... 1093
3231 GATTGCGGCCGGGCGCGATGCCGCCGAAAAGACAGAA...AGCGTTGCCG 3277
1094 .....GlyHisAsnValThrLeuAsnSerGluValLysThrSerA 1107
3278 AACCGGCCCGGCNGGCAGGCGGGGAAAAT..... 3306
1107 snGlySerSerAsnAlaGlyAsnAspAsnSerThrGlyLeuThrIleSer 1123
3307 .....GTCGGCATTATGCAGGCGGAGGAAGAGAAAAAACGGGTGCA 3347
1124 AlaLysAspValThrValAsnAsnIleValThrSerHisLysThrIleAs 1140
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1140 nIleSerAlaAlaAlaGlyAsnValThrThrLysGluGlyThrThrIleA 1157
3398 CGGNTACCACCGCCTTCCCCCGCGCCCGCNGCGCCCGCCGGGATTTGCCG 3447
1157 snAlaThrThrGly.SerValGluValThrAlaGlnAsnGlyThrIleLy 1173
3448 CAACCGCAGCCCCAACCGCAACCTCAACCCCAACCGCAGCGCGACCTGAT 3497
1173 sGlyAsnIleThrSerGlnAsnValThrVal.....ThrAlaThrGluA 1188
3498 NAGCCGTTATGCCAATAGCGGTTTGAGTGAATTTTCCGCCACGCTCAACA 3547
1188 snLeuValThrThrGluAsnAlaValIleAsnAlaThrSerGlyThrVal 1204

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3548 GCGTTTTCGCCGTACAGGACGAATTGGACCGCGTGTTTGCCGAAGACCGC 3597
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1205 AsnIleSer.............................ThrLysThrGl 1211

3598 CGCAACGCNGTTTGGA...CAAGCNGCATCCGGNACACCAAACACTACCG 3644
     :           |||   ::::::::::||||||:::   |||   |||:
1211 yAspIleLysGlyGlyIleGluSerThrSerGlyAsnValAsnIleThrA 1228

3645 TTCGC............AAGATTTCCGCGCCTACCGCCAACAAACCGACC 3682
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3683 TGCGCCAAATCGGTATGCAGAAAAACCTCGGCAGCGGGCGCGTCGGCATC 3732
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1245 ValThrAlaAspAlaGlyAlaLeuThrThrThrAlaGlySerThrIleSe 1261

3733 CTGTTTTCGCACAACCGGA.............................. 3751
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1261 rAla......ThrThrGlyAsnAlaAsnIleThrThrLysThrGlyAspI 1276

3752 .................CCGAAAACANCTTCGACGACGGCATCGGCAACT 3784
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1276 leAsnGlyLysValGluSerSerSerGlySerValThrLeuValAlaThr 1292

3785 CGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAAT............AC 3822
               |||   ::::::   :::|||||||||           .||
1293 GlyAlaThrLeuAlaValGlyAsnIleSerGlyAsnThrValThrIleTh 1309

3823 GGCATCGGCAGGTTCGACATCGGCATCAGCACGGGCGCGGGTTTTAGCAG 3872
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1309 rAlaAspSerGlyLysLeuThrSerThrValGlySerThrIleAsnGlyT 1326

3873 CGGCANTCTNTCAGACGGCATCGGAGGCAAAA.................. 3904
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1326 hrAsnSerValThrThrSerSerGlnSerGlyAspIleGluGlyThrIle 1342

3905 TCCGCCGCCGCGTGCTGCATTACGGCATTCAGGCACGAT...ACCGCGCC 3951
     |||:::   :::      :::||||||          |||   |||
1343 SerGlyAsnThrValAsnValThrAlaSerThrGlyAspLeuThrIleGl 1359

3952 GGTTTCGGCGGATTCGGCATCGAACCGTACATCGGCGCAACGCGCTATTT 4001
        ||||||          :::::::::   :::|||      :::  :
1359 yAsnSerAlaLysValGluAlaLysAsnGlyAlaAlaThrLeuThrAlaG 1376

4002 CGTCCAAAAAGCGGATTACCGCTACGAAAACGTCAATATCG 4042
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1376 luSerGlyLysLeuThrThrGlnThrGlySerSerIleThr 1389
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seq_documentation_block:

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ID   AAB01847 standard; Protein; 1095 AA.
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AC   AAB01847;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain 12 mature HMW1A protein, SEQ ID NO:69.
XX
KW   Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain 12.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52196.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 8; Fig 28F-Q; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   1095 AA;
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alignment_scores:

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           Quality:  254.50              Length:   1062
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 Percent Similarity:  50.565   Percent Identity: 20.433
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alignment_block:

US-09-303-518D-651 x AAB01847 ..

Align seg 1/1 to: AAB01847 from: 1 to: 1095

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   1 ProAspAsnValSerIleAsnAlaGluThrAlaGlyArgSerAsnThrSe 17

 441 GCCTGACAATTCACACCCTTACAACGGCGAT...TANCATATGCCGCGTT 487
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  17 rGluAspAspGluTyrThrGlySerGlyAsnSerAlaSerThrProLysA 34

 488 TGCATAAATTTGTCACAGATGCAGAACCTGTCGAAATGACGAGTGACATG 537
       :::|||      |||            :::   :::   |||   :::
  34 rgAsnLysGluLysThrThrLeuThrAsnThrThrLeuGluSerIleLeu 50

 538 AGGGGGAATACCTATTCCGATAAAGAAAAATATCCCGAGCGTGTCCGCAT 587
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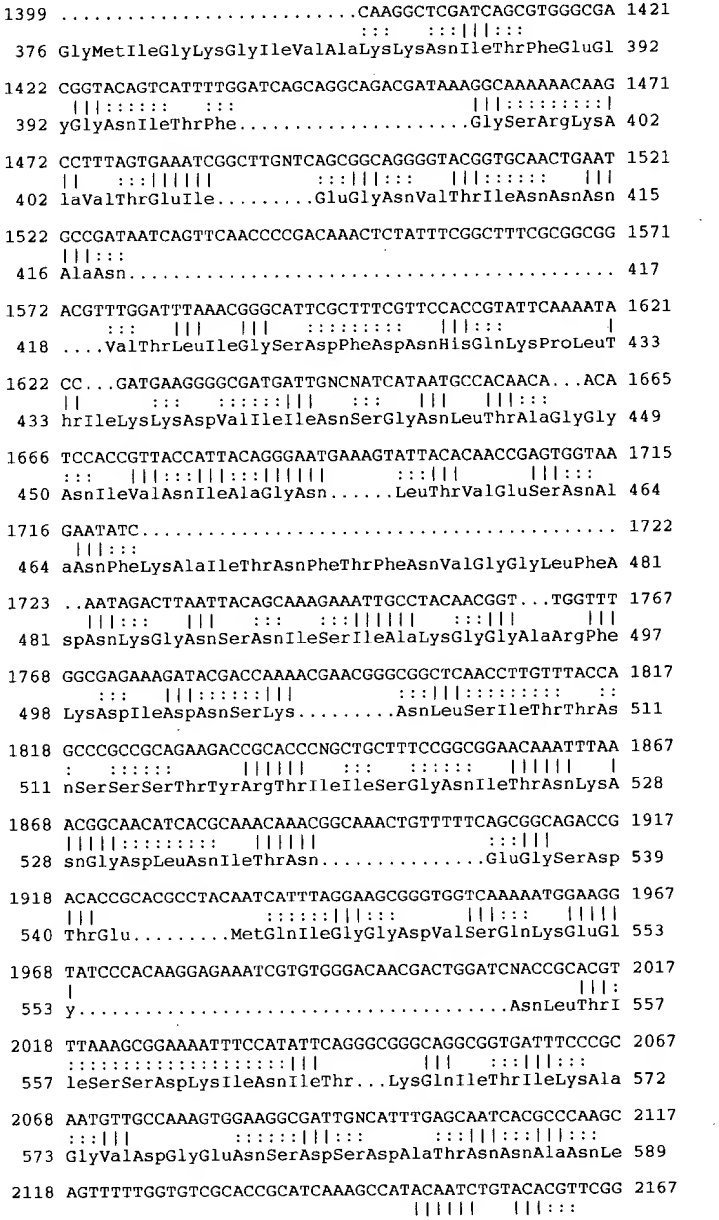

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     |||:::::::::::::|||::::::   ::::::
 603 AsnIleSerGlyPheAsnLysAlaGluIleThrAlaLys..... 615

2268 CNATNACGNTNNTTNAAANCTCNCNGGGCNTGCNNCACTNAANGGCAATC 2317
                              |||:::                |||||
 616 .....................AspGlySerAspLeuThrIleGlyAsnT 625

2318 TT...AGTGCAAATGGCGATACACGTTATACAGTCAGCCACAACGCCACC 2364
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 625 hrAsnSerAlaAspGlyThrAsnAlaLysLysValThrPheAsnGlnVal 641

2365 CAAAACGGCAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATTTAATCA 2414
     :::::::::::::|||      |||                   :::::
 642 LysAspSerLysIleSerAlaAspGly.................HisLy 652

2415 AGCCACATTAAACGGCAACNCATCGGNTTCGGGCAATGCTTCATTTAATC 2464
     ::::||||||:::::::::   ::::::||||||:::   :::   |||
 652 sValThrLeuHisSerLysValGluThrSerGlySerAsnAsn...AsnT 668

2465 TAAGCAACAACGCCGCACAAAACGGCAGTCTGACGCTTTCCGACAACGCT 2514
       ::::::::::::   :::|||::::::||||||:::      :::|||
 668 hrGluAspSerSerAspAsnAsnAlaGlyLeuThrIle......AspAla 682

2515 AAGGCAAACGTAAGCCATTCCGCACTCAACGGCAATGTCTCCCTAGCCGA 2564
     |||   ||||||:::          :::|||:::|||::::::   :::
 683 Lys...AsnValThr.........ValAsnAsnAsnIleThr...SerHi 694

2565 TAAGGCAGTATTCCATTTTGAAAACAGCCGCTTTACCGGACAACTCAGCG 2614
      |||||||||          :::   |||      :::|||::::::::
 694 sLysAlaVal.........SerIleSerAlaThrSerGlyGluIleThrT 708

2615 GCAGCAAGGANACAGCATTACACTTAAAA......GACAGCGAATGGACG 2658
       :::      |||:::::::::             :::   ||| . |||
 708 hrLysThrGlyThrThrIleAsnAlaThrThrGlyAsnValGluIleThr 724

2659 CTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTGACAACGCCACCAT 2708
           :::|||:::   ||||||::::::::   ::::::::::::::
 725 AlaGlnThrGlySerIleLeuGlyGlyIleGluSerSerSerGlySerVa 741

2709 TACACTCAATTCCGCCTATCGCCACGATGCTGCAGGCGCGCAAACCGGCA 2758
     :||||||::::::::::          ::::::|||   |||   ::::::
 741 lThrLeuThrAlaThr.........GluGlyAlaLeuAlaValSerAsnI 755

2759 GNGTGTCAGACACGCCGCGCCGCCGTTCGCGCCGTTCCCTATTATCCGTT 2808
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2809 ACACCGCCAACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGG 2858
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 772 LeuAlaGlySerThrIleLysGlyThrGluSerValThrThrSerSerGl 788

2859 CAAATTGAACNGTCAAGGAACATTC.....................CGCT 2887
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 788 nSerGlyAspIleGlyGlyThrIleSerGlyGlyThrValGluValLysA 805

2888 TTATGTCGGAACTCTTCGGCTACCGAAGCGACAAATTGAAGCTGGCGGAA 2937
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 805 laThrGluSerLeuThrThrGlnSerAsnSerLysIleLys...AlaThr 820

2938 AGTTCCGAAGGNACTTACACCTTGGCGGTC..................... 2967
     ::::::|||::::::   |||   |||:::
 821 ThrGlyGluAlaAsnValThrSerAlaThrGlyThrIleGlyGlyThrIl 837

2968 ....AACAATACCGGCAACGAACCCGTAAGCCTCGATCAATTGACGGTA. 3012
       :::||||||   |||      ::::::      :::||||||||||
 837 eSerGlyAsnThrValAsnValThrAlaAsnAlaGlyAspLeuThrValG 854

3013 .....................GTGGAAGGGAAAGACAACAAACCGCTG 3039
                           :::||||||      :::
 854 lyAsnGlyAlaGluIleAsnAlaThrGluGlyAlaAlaThrLeuThrThr 870

3040 TCCGAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGATGCCGGCGC 3089
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3090 GTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGCATAATC 3139
     ::|||   :::|||   |||||||:::   :::|||   |||      |||
 887 ysGlyGlnValAsnLeuSerAlaGlnAspGlySerValAlaGlySerIle 903

3140 CGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAGAAGCCAAA 3189
     ::::::   |||   ::::::   |||:::::::::            ||
 904 AsnAlaAlaAsnValThrLeuAsnThrThrGlyThrLeuThrThrValLy 920

3190 AAACAGGCGGAAAAAGACAACGCGCAAAGCCTTG 3223
     |:::   :::   ::::::|||      :::|||
 920 sGlySerAsnIleAsnAlaThrSerGlyThrLeu 931
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seq_documentation_block:

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ID   AAB01833 standard; Protein; 1005 AA.
XX
AC   AAB01833;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain K21 mature HMW2A protein, SEQ ID NO:41.
XX
KW   Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain K21.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52182.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 8; Fig 21A-O; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
```

CC the invention contains an A gene modified such that it encodes only the
CC mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC vectors are used for the production of recombinant H. influenzae HMW
CC proteins which can be used as vaccines to mediate a humoral or
CC cell-mediated immune response to provide protection against diseases in
CC humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC antigens in immunoassays for detecting antibodies against Haemophilus,
CC HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC HMW proteins can be used to isolate and clone hmw genes from other
CC non-typeable strains of Haemophilus via hybridisation reactions. The
CC present sequence represents a mature HMWA protein from a non-typeable
CC strain of H. influenzae.
XX
SQ Sequence 1005 AA;

alignment_scores:
Quality: 252.00 Length: 1177
Ratio: 0.451 Gaps: 53
Percent Similarity: 47.494 Percent Identity: 19.031

alignment_block:
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Align seq 1/1 to: AAB01833 from: 1 to: 1005

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 45 GlnLysGlyIleGluValAsnIleSerAlaThrLysAsnValThrValAs 61

276 TTTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAAT 325
    :   :::|||      :::||||||:::   :::|||   :::::::::
 61 nAlaAspValAspValLysAsnGlyThrLeuValLeuHisSerGlnArgA 78

326 ATATTGTGAGCGTGGCACATAACGGCGGCTATAACAACGTTGATTTTGGT 375
        |||::::::      ||||||:::   ::::::::::::   |||
 78 snGlyValLysIle......AsnGlyAsnIleThrSerThrGlnAsnGly 92

376 ............GCGGAAGGAAGNAATCCCGATCAGCACCGTTTTTCTTA 413
                    |||   :::   |||   |||:::
 93 AsnLeuThrIleLysThrGlyGlyLysValAspValHisLysAsnIleTh 109

414 CCAAATTGTGAAAAGAAATAATTATAAGCCTGACAATTCACACCCTTACA 463
        :::          |||         ||||||:::
109 rLeuGlyMetGlyPheLeuAsnIleThrSerAspAsnAsn.......... 122

464 ACGGCGATTANCATATGCCGCGTTTGCATAAATTTGTCACAGATGCAGAA 513
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123 ................................IleThrPheGluLys 127

514 CCTGTCGAAATGACGAGTGACATGAGGGGGAATACCTATTCCGATAAAGA 563
        ::::::|||         :::||||||      |||::::::||
128 GlyAspAsnLeuThrIleThrAlaGlnGlyAsnIleIleSerAsnGlnGl 144

564 AAAATATCCCGAGCGTGTCCGCATCGGCTCA.................... 594
    |:::      :::::::::|||:::::::::
144 uAsn......LysGlnLeuArgPheSerAsnValSerLeuAsnGlyMetG 159

595 ............................GGACACCACTATTGGCGTTAT 615
                                   |||:::|||      ::::::
159 lyAlaGlyLeuThrPheThrAlaAsnLysGlyAsnHisThrHisLysPhe 175

616 GATGATGACAAACACGGCGATTTATCCTACTCCGGCGCATGGTTAATTGG 665
    |||           |||   |||:::   ||||||      :::|||::
176 Asp............GlyThrLeuAsnIleSerGlyLysValValIleAs 188

666 CGGCAATACA......CATATGCAGGGTTGGGGAAATAATGGCGTANTTA 709
    :   :::|||      ::::::      |||:::   :::
188 nGlnThrThrProHisAsnIleAlaProTrpAsnAlaSer.......... 201

710 GTTTGAGCGGCGATGTGCGCCATGCCAACGACTATGGCCCTATGCCGATT 759
                              |||::::::|||      :::
202 .......................AlaAspSerTyrTrpAsnValThrThr 210

760 GCAGGTGCGGCAGGCGACAGCGGTTCGCCAATGTTTATTTATGACAAAAC 809
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211 LeuThrLeuGlyAsnAsnAlaGlnPheThrPheIleLysPheValAspSe 227

810 AAACAATAAATGGCTGCTCAACGGAGTTTTACAAACC......GGCTACC 853
    :|||::::::      ||||||:::      ::::::     |||
227 rAsnArgSerValAlaLeuAsnSerGlySerArgSerPheAlaGlyValL 244

854 CTTATTCCGGCAGGGAAAACGGTTTCCAGCTGATACGCAAAGATTGGTTC 903
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244 ysPheTyrGlyLysAsnAsnGluMetLys..................... 253

904 TACGATGACATTTACAGAGGCGATACACATACCGTCTNTTTTGAACCGCG 953
            :::      |||||||:::   :::|||   |||:::   ::
254 .........PheAsnIleGlyAspAsnAlaAsnValGluPheLysLeuLy 267

954 CAGTAACGGACATTTTTCCTTTACATCCAACAAC.............. 987
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267 sSerAsnAspAsn.........ThrSerAsnAsnLysProLeuProIleG 281

988 ......................AACGGTACGGGTACGGTAACA...... 1008
                            :::|||:::||||||||||:::
281 lnPheLeuSerAsnIleSerAlaThrGlyAsnGlyThrValSerPheAsp 297

1009 ...GAAACCAACGAAAAGGTNTCCAATCCAAAGCTTAAAGTACAGACAGT 1055
       :::::::|||   ::::::   :::   :::|||:::::::::   ::
298 IleHisAlaAsnLeuSerAlaArgSerThrGluLeuAsnMetSerLeuIl 314

1056 CCGACTG.........TTTGACGAATCTTTGAAT................ 1080
     :::::::            :::   |||:::|||
314 eAsnIleSerAsnGlyValAsnPheSerIleAsnSerHisValArgGlyA 331

1081 ...........GAAACTGATAAAGAACCAGTTTACGCGGCAGGGGGTGTT 1119
               |||       |||:::   :::       |||   |||
331 snAsnAlaPheGluIleLysLysAspLeuIleIleAsnAlaThrGlySer 347

1120 AAT............CAGTACCGTCCAAGGTTAAACAACGGTGAAAACCT 1157
     |||             |||   :::   :::::::::|||
348 AsnPheAsnLeuLysGlnThrLysAspLysPheAspAsn........... 360

1158 TTCTTTTATCGATTACGGCAACGGCAAACTCATCTTATCAAACAACATCA 1207
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361 ..........SerTyrGluLysAsnAlaIlePheSerThrHisAsnLeuT 374

1208 ACCAAGGCGCGGGCGGTTTGTATTTTGAAGGTGATTTTACGGTCTCGCCT 1257
     ::                      :::   |||:::   |||::::::
374 hr..................IleLeuGlyGlyAsnValThrLeuGlyGly 384

1258 GAAAACAACGAAACGTGGCAAGGCGCGGGCGTTCATATCAGTGAAGACAG 1307
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385 GluAsnSerSerSerAsnIleLysGlyAsnIleAsnIleAsnSerLysAl 401

1308 TACCGTTACTTGGAAAGTAAACGGCGTGGCAAACGACCGCCTGTCCAAAA 1357
     :::::||||||   ::::::::::::
401 aAsnValThrLeuGlnAlaHisAla.......................... 409

1358 TCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGGGAAAACCAAGGCTCG 1407
               ||||||   |||::::::   |||          :::   :::
410 ........GlyThrSerHisLeuAspLysLys.........GluArgThr 420

1408 ATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCAGGCAGACGATAA 1457
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421 LeuThrLeuGlyAsnValSerVal.......................... 428

1458 AGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGNTCAGCGGCAGGGGTA 1507

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1508 CGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAACTCTATTTC 1557
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 428 ..................................................... 428

1558 GGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCTTTCGTTCCA 1607
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 429 .........GlyGlyAsnLeuAsnIleIleGly..................... 436

1608 CCGTATTCAAAATACCGATGAAGGGGCGATGATTGNCNATCATAATGCCA 1657

 436 ..................................................... 436

1658 CAACAACATCCACCGTTACCATTACAGGGAATGAAAGTATTACACAACCG 1707
            |||::::::   |||   ||||||   ||||||:::::
 437 ........SerAsnAlaHisIleAspGlyAsnLeuSerIleAlaGluSer 450

1708 AGT.........GGTAAGAATATCAATAGACTTAATTACAGCAAAGAAAT 1748
     :::          ||||||:::   |||:::||||||   :::    ::
 451 AlaLysPheGlnGlyLysThrAsnAsnAsnLeuAsnIleThrGlyThrPh 467

1749 TGCCTACAACGGTTGGTTTGGC.......................... 1770
     ::::   ||||||
 467 eThrAsnAsnGlyThrAlaAspIleAsnIleLysGlnGlyValValLysL 484

1771 ..GAGAAAGATACGACCAAAACGAACGGGCGGCTCAACCTTGTTTACCAG 1818
       :::   |||   |||   :::|||||:::||||||::::::   :::
 484 euGlnGlyAspIleThr...AsnAsnGlyAsnLeuAsnIleThrThrAsn 499

1819 CCCGCCGCAGAAGACCGCACCCNGCTGCTTTCCGGCGGAACAAATTTAAA 1868
        :::::::::::::::|||                    :::||
 500 AlaSerValAsnGlnLysThrIle.....................IleAs 509

1869 CGGCAACATCACGCAAACAAACGGCAAACTGTTTTTCAGCGGCAGACCGA 1918
     ||||||||||||||:::   :::|||   |||   ::::::        :
 509 nGlyAsnIleThrAsnLysLysGlyAspLeuAsnIleLysAspIleLysA 526

1919 CACCGCACGCCTACAATCATTTAGGAAGCGGGTGGTCAAAAATGGAAGGT 1968
     ::   :::|||      ::::::|||::::::   |||:::   ||||||
 526 la...AsnAlaGluIleGlnIleGlyGlyAsnIleSerGlnLysGluGly 541

1969 ATCCCACAAGGAGAAATCGTGTGGGACAACGACTGGATCNACCGCACGTT 2018

 541 ..................................................... 541

2019 TAAAGCGGAAAATTTCCATATTCAGGGCGGGCAGGCGGTGATTTCCCGCA 2068
               |||:::   |||::::::   :::      |||:::::::
 542 ..........AsnLeuThrIleSerSerAspLysIleAsnIleThrLysA 555

2069 ATGTTGCCAAAGTGGAAGGCGATTGNCATTTGAGCAATCACGCCCAAGCA 2118
     :::::   :::::::::::::|||:::      :::|||      :::
 555 rgIle...GluIleLysAlaAspThrAspGlnGlyAsnSerAspSer... 569

2119 GTTTTTGGTGTCGCACCGCATCAAAGCCATACAATCTGTACACGTTCGGA 2168
           |||||||||   :::   :::   ||||||   |||:::
 570 ......GlyValAlaSerAsnAlaAsnLeuThrIleLysThrLys..... 582

2169 CTGGACNGGTCTGACAAATTGTGTCGAANAAANCATTACCGACGATAAAG 2218
                          |||   ::::::||||||:::
 583 ........................GluLeuThrLeuThrAspAsnLeuA 591

2219 TGATTGCTTCATTGACTAAGACNGACNTNAGCGGCANTGTNAGNCTNNCC 2268
       |||:::::::::::::|||::::::   ::::::
 591 snIleSerGlyPheAsnLysAlaGluIleThrAlaLys............. 603

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 604 ......................AspAsnSerAspLeuIleIleGlyLysAl 613

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2369 ACGGCAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATTTAATCAA... 2415
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2416 ...GCCACATTAAAC.............GGCAACNCATCGGNTTCGGG 2447
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2448 CAATGCTTCATTTAATCTAAGC.......................... 2469
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2470 ..................AACAACGCCGCACAAAACGGCAGTCTGACG 2499
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 679 leThrSerHisLysThrValAsnIleSerAlaSerGluGlyGlyIleThr 695

2500 CTTTCCGACAACGCTAAGGCAAACGTAAGCCATTCCGCACTCAACGGCAA 2549
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 696 ............ThrLysAlaGlyThrThrIleAsnAlaThrThrGlySe 708

2550 TGTCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAACAGCCGCTTTA 2599
     :|||::::::::::   |||                          |
 708 rValGluValThrAlaLys............................T 715

2600 CCGGACAACTCAGCGGCAGC.........AAGGANACAGCATTACACTTA 2640
     |||||:::::|||||||:::          |||:::::::::::::
 715 hrGlyAspIleSerGlyThrIleSerGlyLysThrValSerValThrAla 731

2641 AAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAA 2690
           ::::::   |||:::   :::|||:::::::::   |||   ::
 732 ThrThrAspSerLeuThrValLysGlyGlyAlaLysIle...AsnAlaTh 747

2691 CCTTGACAACGCCACCATTACACTCAAT..................... 2718
     :      :::|||||||:::|||   :::
 747 rGluGlyThrAlaThrLeuThrAlaSerSerGlyLysLeuThrThrGluA 764

2719 ..............TCCGCCTATCGCCACGATGCTGCAGGCGCGCAAACC 2754
                    |||:::   :::      :::|||::::::|||:::
 764 laAsnSerAlaIleSerGlyAlaAsnGlyValThrAlaSerSerGlnSer 780

2755 GGCAGNGTGTCAGACACGCCGCGCCGCCGTTCGCGCCGTTCCCTATTATC 2804
     |||   :::|||   |||         ::::::
 781 GlyAspIleSerGlyThrIleSerGlyLysThr.................. 791

2805 CGTTACACCGCCAACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAA 2854
                  :::||||||   :::      ::::::||||||||||:
 792 .............ValSerValThrAlaSerSerGlySerLeuThrValG 804

2855 ACGGC......AAATTGAAC...NGTCAAGGAACATTCCGCTTTATGTCG 2895
     ::|||      |||:::|||   ::::::|||:::      :::   :::
 804 lyGlyAspAlaLysIleAsnAlaThrGluGlyAlaAlaThrLeuThrAla 820

2896 GAACTCTTCGGCTACCGAAGCGACAAATTGAAGCTGGCGGAAAGTTCCGA 2945
                       :::   |||   :::      ::::::::::||
 821 ThrLysGlyThrLeuThrThrValLysGlySerAsnIleAspAlaAsnGl 837

2946 AGGNACTTACACCTTG...GCGGTCAACAATACCGGCAACGAACCCGTAA 2992
     |||||||   ::::::   |||   :::   |||   |||       :::|
 837 uGlyThrLeuValIleAsnAlaGlnAspAlaThrLeuAsnGlyAspAlaS 854

2993 GCCTCGATCAATTGACGGTA............GTGGAAGGGAAAGACAAC 3030
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 854 erGlyAspArgThrGluValAsnAlaValAsnAlaSerGlySerGlyAsn 870

3031 ......AAACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAACA 3074
                  |||::::::::::|||:::|||   :::   :::
 871 ValThrAlaLysThrSerSerSerValAsnIleThrGlyAspLeuSerTh 887

3075 CGTCGATGCCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGT 3124
          :::::::::              :::::|||   |||:::|||:::
 887 rIleAsnGly............LeuAsnIleIleSerLysAsnGlyLys. 899

3125 TCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGC 3174
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 900 ..........AsnThrVal....................ValLeuLys 905
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    3175 AAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTGA 3224
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     906 GlyAlaGluIleAspValLysTyrIleGlnProGlyValAlaSerAlaAs 922

    3225 CGCGCTGATTGCGGCCGGGCGCGATGCCGCCGAAAAGACAGAAAGCGTTG 3274
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     922 nGluValIleGluAlaLysArg...AlaLeuGluLysValLysAspLeuS 938

    3275 CCGAACCGGCCCGGCNGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCG 3324
         :::::      |||   :::   ::::::   :::|||:::      :::
     938 erAspGluGluArgGluThrLeuAlaLys...LeuGlyValSerAlaVal 953

    3325 GAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACAGCGCNTTGGCGAA 3374
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     954 ............ArgPheIleGluProAsnAsnThrIleThrValAsnTh 966

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     966 rGlnAsnGluPheThrThrArgProSerSer 976
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ID   AAB01832 standard; Protein; 1011 AA.
XX
AC   AAB01832;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain K21 HMW2A protein, SEQ ID NO:39.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain K21.
XX
PN   WO200020609-A2.
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PD   13-APR-2000.
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PA   (CONN-) CONNAUGHT LAB LTD.
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PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52181.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 12; Fig 21A-O; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
XX
SQ   Sequence   1011 AA;
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             Ratio:  0.451                 Gaps:     53
 Percent Similarity:  47.494   Percent Identity: 19.031

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      51 GlnLysGlyIleGluValAsnIleSerAlaThrLysAsnValThrValAs 67

     276 TTTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAAT 325
         :   :::|||      :::||||||:::   :::|||   :::::::::
      67 nAlaAspValAspValLysAsnGlyThrLeuValLeuHisSerGlnArgA 84

     326 ATATTGTGAGCGTGGCACATAACGGCGGCTATAACAACGTTGATTTTGGT 375
             |||::::::      ||||||:::   ::::::::::::   |||
      84 snGlyValLysIle......AsnGlyAsnIleThrSerThrGlnAsnGly 98

     376 ............GCGGAAGGAAGNAATCCCGATCAGCACCGTTTTTCTTA 413
                        |||   :::   |||   |||:::
      99 AsnLeuThrIleLysThrGlyGlyLysValAspValHisLysAsnIleTh 115

     414 CCAAATTGTGAAAAGAAATAATTATAAGCCTGACAATTCACACCCTTACA 463
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     115 rLeuGlyMetGlyPheLeuAsnIleThrSerAspAsnAsn..... 128

     464 ACGGCGATTANCATATGCCGCGTTTGCATAAATTTGTCACAGATGCAGAA 513
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     129 .................................IleThrPheGluLys 133

     514 CCTGTCGAAATGACGAGTGACATGAGGGGGAATACCTATTCCGATAAAGA 563
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     134 GlyAspAsnLeuThrIleThrAlaGlnGlyAsnIleIleSerAsnGlnGl 150

     564 AAAATATCCCGAGCGTGTCCGCATCGGCTCA.................. 594
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     150 uAsn......LysGlnLeuArgPheSerAsnValSerLeuAsnGlyMetG 165

     595 ............................GGACACCACTATTGGCGTTAT 615
                                        |||:::|||      ::::::
     165 lyAlaGlyLeuThrPheThrAlaAsnLysGlyAsnHisThrHisLysPhe 181

     616 GATGATGACAAACACGGCGATTTATCCTACTCCGGCGCATGGTTAATTGG 665
         |||            |||   |||:::   ||||||      :::|||::
     182 Asp............GlyThrLeuAsnIleSerGlyLysValValIleAs 194

     666 CGGCAATACA......CATATGCAGGGTTGGGGAAATAATGGCGTANTTA 709
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     194 nGlnThrThrProHisAsnIleAlaProTrpAsnAlaSer..... 207
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 208 ......................AlaAspSerTyrTrpAsnValThrThr 216

 760 GCAGGTGCGGCAGGCGACAGCGGTTCGCCAATGTTTATTTATGACAAAAC 809
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 217 LeuThrLeuGlyAsnAsnAlaGlnPheThrPheIleLysPheValAspSe 233

 810 AAACAATAAATGGCTGCTCAACGGAGTTTTACAAACC......GGCTACC 853
     :|||:::::      |||||||:::     ::::::      |||
 233 rAsnArgSerValAlaLeuAsnSerGlySerArgSerPheAlaGlyValL 250

 854 CTTATTCCGGCAGGGAAAACGGTTTCCAGCTGATACGCAAAGATTGGTTC 903
       :::    |||:::::|||    ::::::
 250 ysPheTyrGlyLysAsnAsnGluMetLys..................... 259

 904 TACGATGACATTTACAGAGGCGATACACATACCGTCTNTTTGAACCGCG 953
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 260 .........PheAsnIleGlyAspAsnAlaAsnValGluPheLysLeuLy 273

 954 CAGTAACGGACATTTTTCCTTTACATCCAACAAC................ 987
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 273 sSerAsnAspAsn.........ThrSerAsnAsnLysProLeuProIleG 287

 988 ......................AACGGTACGGGTACGGTAACA...... 1008
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 287 lnPheLeuSerAsnIleSerAlaThrGlyAsnGlyThrValSerPheAsp 303

1009 ...GAAACCAACGAAAAGGTNTCCAATCCAAAGCTTAAAGTACAGACAGT 1055
        ::::::|||   ::::::   :::   :::|||:::::::::   ::
 304 IleHisAlaAsnLeuSerAlaArgSerThrGluLeuAsnMetSerLeuIl 320

1056 CCGACTG.........TTTGACGAATCTTTGAAT................ 1080
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1081 ..........GAAACTGATAAAGAACCAGTTTACGCGGCAGGGGGTGTT 1119
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 337 snAsnAlaPheGluIleLysLysAspLeuIleIleAsnAlaThrGlySer 353

1120 AAT............CAGTACCGTCCAAGGTTAAACAACGGTGAAAACCT 1157
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 354 AsnPheAsnLeuLysGlnThrLysAspLysPheAspAsn........... 366

1158 TTCTTTTATCGATTACGGCAACGGCAAACTCATCTTATCAAACAACATCA 1207
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 367 ..........SerTyrGluLysAsnAlaIlePheSerThrHisAsnLeuT 380

1208 ACCAAGGCGCGGGCGGTTTGTATTTTGAAGGTGATTTTACGGTCTCGCCT 1257
     ::
 380 hr.................IleLeuGlyGlyAsnValThrLeuGlyGly 390
                        :::    |||:::    |||::::::

1258 GAAAACAACGAAACGTGGCAAGGCGCGGGCGTTCATATCAGTGAAGACAG 1307
     ||||||:::::::::            ::::::::::::|||::::::    ::
 391 GluAsnSerSerSerAsnIleLysGlyAsnIleAsnIleAsnSerLysAl 407

1308 TACCGTTACTTGGAAAGTAAACGGCGTGGCAAACGACCGCCTGTCCAAAA 1357
     :::::||||||   ::::::::::::
 407 aAsnValThrLeuGlnAlaHisAla........................ 415

1358 TCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGGGAAAACCAAGGCTCG 1407
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 416 ........GlyThrSerHisLeuAspLysLys.........GluArgThr 426

1408 ATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCAGGCAGACGATAA 1457
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 427 LeuThrLeuGlyAsnValSerVal......................... 434

1458 AGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGNTCAGCGGCAGGGGTA 1507

 434 ................................................. 434

1508 CGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAACTCTATTTC 1557

 434 ................................................. 434

1558 GGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCTTTCGTTCCA 1607
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 435 .........GlyGlyAsnLeuAsnIleIleGly................. 442

1608 CCGTATTCAAAATACCGATGAAGGGGCGATGATTGNCNATCATAATGCCA 1657

 442 ................................................. 442

1658 CAACAACATCCACCGTTACCATTACAGGGAATGAAAGTATTACACAACCG 1707
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1708 AGT.........GGTAAGAATATCAATAGACTTAATTACAGCAAAGAAAT 1748
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1749 TGCCTACAACGGTTGGTTTGGC............................ 1770
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 473 eThrAsnAsnGlyThrAlaAspIleAsnIleLysGlnGlyValValLysL 490

1771 ..GAGAAAGATACGACCAAAACGAACGGGCGGCTCAACCTTGTTTACCAG 1818
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1819 CCCGCCGCAGAAGACCGCACCCNGCTGCTTTCCGGCGGAACAAATTTAAA 1868
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 506 AlaSerValAsnGlnLysThrIle....................IleAs 515

1869 CGGCAACATCACGCAAACAAACGGCAAACTGTTTTTCAGCGGCAGACCGA 1918
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 515 nGlyAsnIleThrAsnLysLysGlyAspLeuAsnIleLysAspIleLysA 532

1919 CACCGCACGCCTACAATCATTTAGGAAGCGGGTGGTCAAAAATGGAAGGT 1968
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 532 la...AsnAlaGluIleGlnIleGlyGlyAsnIleSerGlnLysGluGly 547

1969 ATCCCACAAGGAGAAATCGTGTGGGACAACGACTGGATCNACCGCACGTT 2018

 547 ................................................. 547

2019 TAAAGCGGAAAATTTCCATATTCAGGGCGGGCAGGCGGTGATTTCCCGCA 2068
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2069 ATGTTGCCAAAGTGGAAGGCGATTGNCATTTGAGCAATCACGCCCAAGCA 2118
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 561 rgIle...GluIleLysAlaAspThrAspGlnGlyAsnSerAspSer... 575

2119 GTTTTTGGTGTCGCACCGCATCAAAGCCATACAATCTGTACACGTTCGGA 2168
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 576 ......GlyValAlaSerAsnAlaAsnLeuThrIleLysThrLys..... 588

2169 CTGGACNGGTCTGACAAATTGTGTCGAANAAANCATTACCGACGATAAAG 2218
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 610 .....................AspAsnSerAspLeuIleIleGlyLysAl 619

2319 TAGTGCAAATGGCGATACACGTTATACAGTCAGCCACAACGCCACCCAAA 2368
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 619 aSerSerAspAsnSerAsnAlaLysGlnIleThrPheAspLysValLysA 636

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 652 ValGluThrSerAsnSerAspGlySerThrGlyAsnGlySerAspAspAs 668

2448 CAATGCTTCATTTAATCTAAGC............................ 2469
     :|||   ::::::::::::|||
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2470 ...................AACAACGCCGCACAAAACGGCAGTCTGACG 2499
                         |||   :::|||:::::::|||:::::|||
 685 leThrSerHisLysThrValAsnIleSerAlaSerGluGlyGlyIleThr 701

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 702 ............ThrLysAlaGlyThrThrIleAsnAlaThrThrGlySe 714

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 714 rValGluValThrAlaLys............................T 721

2600 CCGGACAACTCAGCGGCAGC.........AAGGANACAGCATTACACTTA 2640
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2691 CCTTGACAACGCCACCATTACACTCAAT..................... 2718
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2896 GAACTCTTCGGCTACCGAAGCGACAAATTGAAGCTGGCGGAAAGTTCCGA 2945
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2946 AGGNACTTACACCTTG...GCGGTCAACAATACCGGCAACGAACCCGTAA 2992
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3075 CGTCGATGCCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGT 3124
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 893 rIleAsnGly............LeuAsnIleIleSerLysAsnGlyLys. 905

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               |||   |||                          |||
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3175 AAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTGA 3224
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     :::::      |||   :::   ::::::   :::|||:::      :::
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3325 GAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACAGCGCNTTGGCGAA 3374
                  :::   ::::::   ::::::      ::::::
 960 .............ArgPheIleGluProAsnAsnThrIleThrValAsnTh 972

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seq_documentation_block:

ID AAB01837 standard; Protein; 1073 AA.
XX
AC AAB01837;
XX
DT 11-SEP-2000 (first entry)
XX
DE Haemophilus influenzae strain LCDC2 mature HMW2A protein, SEQ ID NO:49.
XX
KW Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW recombinant production; Escherichia coli; antibacterial; vaccine;
KW human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW detection; diagnosis.
XX
OS Haemophilus influenzae strain LCDC2.
XX
PN WO200020609-A2.
XX
PD 13-APR-2000.
XX
PF 07-OCT-1999; 99WO-CA00938.
XX
PR 07-OCT-1998; 98US-0167568.
PR 08-DEC-1998; 98US-0206942.
XX
PA (CONN-) CONNAUGHT LAB LTD.
XX
PI Loosmore SM, Yang Y, Klein MH;
XX
DR WPI; 2000-303789/26.
DR N-PSDB; AAA52186.
XX
PT Nucleic acid molecule for producing recombinant high molecular weight
PT proteins of Haemophilus which are used as a vaccine to provide
PT protection against Haemophilus induced diseases in humans -
XX
PS Claim 8; Fig 23A-P; 307pp; English.
XX
CC The invention relates to the recombinant production of Haemophilus
CC influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC expression construct used to effect recombinant expression comprises a
CC promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
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CC responsible for post-translational processing and secretion of the HMWA
CC proteins. The modified hmwABC operon used in the expression construct of
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```
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
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CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   1073 AA;


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           :::   ||||||:::|||   |||:::|||:::
     153 leAlaGlnGlyThrIleThrLeuThrGlyGluAsn.............. 164

    1039 CTTAAAGTACAGACAGTCCGACTGTTTGACGAATCTTTGAATGAAACTGA 1088
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    1089 TAAAGAACCAGTTTACGCGGCAGGGGGTGTTAATCAGTACCGTCCAAGGT 1138

     177 ..................................................... 177

    1139 TAAACAACGGTGAAAACCTTTCTTTTATCGATTACGGCAACGGCAAACTC 1188
                                           |||||||||
     178 ..................................GlyAsnGlyLeuSer 182

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         |||:::|||:::      |||   :::          |||   :::
     183 IleIleSerThrAlaSerAsnLeuSerHisArgLeuAspGlyGluIleAs 199

    1230 TTTTGAAGGTGATTTTACGGTC.........TCGCCTGAAAACAACGAAA 1270
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     199 nValSerGlyAsnValThrIleAsnGlnThrThrGlnGlnAsnIleGluT 216

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     299 eGlnSerAsnIleSerValSerGlyGlyGlyArgValAsnIleAsnThrL 316

    1388 AAGGGGAAAACCAAGGC.......................TCGATCAGC 1413
           ::::::      |||                       ||||||:::
     316 euAlaAsnLeuThrGlyGlyGlyValGluIleArgSerSerSerIleAsn 332

    1414 GTGGGCGACGGT...ACAGTCATTTTGGATCAGCAGGCAGACGATAAAGG 1460
         |||:::||||||   |||:::   :::      ||||||   |||:::::
     333 ValSerAspGlySerThrLeuSerMetThrAlaGlnAlaArgAspArgAs 349

    1461 CAAAAAACAAGCCTTTAGTGAAATCGGCTTGNTCAGCGGCAGGGGTACGG 1510
         :      :::      :::::::::   :::   :::::::::::::::
     349 nAlaPheGluIleThrLysAspLeuValIleAsnAlaSerAsnSerAsnL 366

    1511 TGCAACTG.........................................AAT 1521
         ::::::::                                        |||
     366 euSerIleIleGlnGlnAsnAspGlyPheAspAsnAsnGlnLysAlaAsn 382

    1522 GCCGATAATCAGTTCAACCCCGACAAACTCTATTTCGGCTTTCGCGGCGG 1571
         |||   |||            ::::||            ::::::||||
     383 AlaIleAsn............SerLysTyrAsnValThrIleGlnGlyGl 395

    1572 ACGTTTGGATTTAAACGGGCATTCGCTTTCGTTCCACCGTATTCAAAATA 1621
         |::::::   |||:::|||                          ||||||:
     395 yAsnValThrLeuGlyGly.......................GlnAsnS 404

    1622 CCGATGAAGGGGCGATGATTGNCNATCATAATGCCACAACAACATCCACC 1671
         ::                          :::::::|||   |||::::::
     404 er.........................SerSerThrIleThrGlySer 411

    1672 GTTACCATTACAGGGAATGAAAGTATTACACAACCGAGTGGTAAGAATAT 1721
         |||:::|||   :::|||   ::::::|||
     412 ValAsnIleGlyAlaAsnAlaAsnValThrLeuGln.............. 423

    1722 CAATAGACTTAATTACAGCAAAGAAATTGCCTACAACGGTTGGTTTGGCG 1771
                                     |||:::||||||      ::::
     424 ..........................AlaHisAsnGly......AsnA 429

    1772 AGAAAGATACGACCAAAACGAACGGGCGGCTCAACCTTGTTTACCAGCCC 1821
         ::::::::         |||   |||::::::::::::
     429 spArgAsnLysLysLeuThrPheGlyAsnValSerVal............ 441

    1822 GCCGCAGAAGACCGCACCCNGCTGCTTTCCGGCGGAACAAATTTAAACGG 1871
               |||   :::      |||:::::::::::::::|||:::|||::
     442 ......GluGlyGluLeuArgLeuValGlyAlaSerAlaAsnIleAsnAs 456

    1872 CAACATCACG.........................CAAACAAACGGCA 1894
         :|||::::::                        :::||||||   :
     456 nAsnLeuSerValLysSerGlyAlaLysPheLysAlaGluThrAsnAspA 473

    1895 AACTGTTTTTCAGCGGCAGACCGACACCGCACGCCTACAAT......CAT 1938
```

```
    ::|||   ::::::|||      |||   ::::::   :::
 473 snLeuAsnIleThrGlyThrPheThrAsnAsnGlyThrSerIleIleAsp 489

1939 TTAGGAAGCGGGTGGTCAAAAATGGAAGGTATCCCACAAGGAGAAATCGT 1988
     :::   :::|||   :::|||:::              |||:::|||::
 490 ValLysLysGlyAlaAlaLysLeu.............GlyAsnIleTh 501

1989 GTGGGACAACGACTGGATCNACCGCACGTTTAAAGCGGAAAATTTCCATA 2038
     :   |||::::::   :::      |||   :::|||:::|||
 501 rAsnAspGlyAsn...LeuAsnIleThrThrAsnAlaLysAsn..... 514

2039 TTCAGGGCGGGCAGGCGGTGATTTCCCGCAATGTTGCCAAAGTGGAAGGC 2088
          |||   ::::::||||||:::   |||:::::::::   :::|||
 515 .....GlyGlnLysSerValIleAsnGlyAsnIleThrAsnAsnLysGly 529

2089 GATTGNCATTTGAGCAATCACGCCCAA.............GCAGTTTTTGG 2126
           :::::::::|||::::::::::              :::   ||
 530 AlaLeuAsnIleThrAsnAsnGlyAsnAspThrGluIleGlnIleGlyGl 546

2127 TGTCGCACCGCATCAAAGCCATACAATCTGTACACGTTCGGACTGGACNG 2176
     |          :::::::::   ::::::         ||||||      :
 546 yAsnIleSerGlnLysGluGlyAsnLeuThrIleSerSerAspLysIleA 563

2177 GTCTGACAAATTGTGTCGAANAAANCATT...ACCGAC............ 2211
     :::::|||:::   :::|||            ||||||
 563 snIleThrLysArgIleGluIleLysAlaGlyThrAspGlnGlyAsnSer 579

2212 GATAAAGTGATTGCTTCA............................TT 2231
     |||:::   :::||||||                            ||
 580 AspSerGlyValAlaSerAsnAlaAsnLeuThrIleLysThrLysGluLe 596

2232 GACTAAGACNGACNTNAGCGGCANTGTNAGNCTNNCCNATNACGNTNNTT 2281
     |      |||:::      :::       :::      :::
 596 uLysLeuThrGluAsnLeuAsnIleSerGlyPheAspLysAlaGluIleV 613

2282 NAAANCTCNCNGGGCNTGCNNCACTNAANGGCAATCTTAGTGCAAATGGC 2331
       :::      :::         :::   ||||||   ::::::::::::
 613 alAlaLysGluAsnAsnAsnLeuIleIleGlyAsnAsnAsnGlyAspAsn 629

2332 GATACACGTTATACAGTCAGCCACAACGCCACCCAAAACGGCAACCTTAG 2381
        :::      |||||||::   |||   ::::::::::::::::||
 630 AlaAsnAlaLysThrValThrPheAsnAsnValLysAspSerLysIleSe 646

2382 CCTCGTGGGCAATGCCCAAGCAACATTTAATCAA......GCCACATTAA 2425
     |      |||:::   ::::::|||:::|||:::         |||  :
 646 rAlaAsnGlyHis...AsnValThrLeuAsnSerLysValGluThrSerA 662

2426 ACGGCAACNCATCGGNTTCGGGCAATGCTTCATTTAATCTA....... 2466
     ::||||||:::::::::::::||||||::::::   |||
 662 spGlyAsnSerAsnThrGluGlyAsnSerAspAsnAsnAlaGlyLeuThr 678

2467 ......AGCAACAACGCCGCACAAAACGGC..................... 2490
           ::::::|||::::::   |||:::
 679 IleAspAlaLysAsnValThrValAsnAsnAspIleThrSerHisLysTh 695

2491 ....AGTCTGACGCTTTCCGAC......AACGCTAAGGCAAACGTAAGCC 2530
         :::::::|||   |||:::      :::::::||||||:::::::::
 695 rValAsnIleThrAlaSerGluArgIleAspThrLysAlaAspThrThrI 712

2531 ATTCCGCACTCAACGGCAATGTCTCCCTA...................... 2559
       :::|||   :::|||||||||:::|||
 712 leAsnAlaThrThrGlyAsnValLysLeuThrAlaValThrSerAspIle 728

2560 ..............GCCGATAAGGCAGTATTCCATTTTGAAAACAGCCG 2594
                    ::::::::::::      ::::::   :::|||
 729 GlnGlyGlyIleLysSerAsnSerGlyAspValAsnIleThrThrSer.. 744

2595 CTTTACCGGACAACTCAGCGGC.........AGCAAGGANACAGCATTAC 2635
         ||||||::::::::::|||         ||||||:::   ::::::
 745 ....ThrGlySerIleAsnGlyLysIleGluSerLysSerGlySerValT 760

2636 ACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAAT 2685
       |||      :::|||   ||||||               :::||||||
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 760 hrLeuThrAlaThrGluLysThrLeu.............ThrValGlyAsn 772

2686 TTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGA 2735
     ::::::   ::::::::::|||:::|||   |||   :::
 773 ValSerGlyAsnThrValThrValThrAlaAsnArgGlyAlaLeuThrTh 789

2736 TGCTGCAGGCGCGCAA...ACCGGCAGNGTGTCAGACACGCCGCGCCGCC 2782
          |||||||:::      :::|||:::   :::   |||        :
 789 rLeuAlaGlySerThrIleAsnGlyThrAsnGlyValThrThrSerSerG 806

2783 GTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACT...TCGGTAGAA 2829
     ::|||   :::         :::||||||      |||   ||||||
 806 lnSerGlyGluIleGlyGlyGluValThrGlyLysThrValSerValThr 822

2830 TCCCGTTTCAACACGCTGACGGTAAACGGC......AAATTGAAC...NG 2870
     :::      ::::::||||||||||:::|||      |||:::|||   ::
 823 AlaThrAlaGlySerLeuThrValLysGlyGlyAlaLysIleAsnAlaTh 839

2871 TCAAGGAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGAAGCGACA 2920
     ::::||||||      :::   ::::::               |||   |
 839 rGluGlyThrAlaThrLeuThrAlaSer..............SerGlyL 851

2921 AATTGAAGCTGGCGGAAAGTTCCGAAGGNACT.................. 2952
     |||||            ||||||:::   |||
 851 ysLeuThrThrGluAlaSerSerAsnIleThrSerAlaLysGlyGlnVal 867

2953 .............................................TACAC 2957
                                                    ::
 868 AspLeuSerAlaGlnAspGlySerIleAlaGlyGlnIleSerAlaAlaAs 884

2958 CTTGGCGGTCAACAATACCGGCAACGAACCCGTAAGCCTCGATCAATTGA 3007
     ::::::::::|||:::||||||:::                    ||||
 884 nValThrLeuAsnThrThrGlyThr.....................LeuT 894

3008 CGGTAGTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTC 3057
     ||:::||||||  |||::::::   |||            |||||||:::
 894 hrThrValGlu.GlySerSerIleAsnAlaAsnGluGlyThrLeuValIl 910

3058 ACCCTGC.....................AAAACGAACACGTCGATGCCGG 3086
        :::                     |||::::::   :::
 910 eAsnAlaAsnAspAlaLysLeuAspGlyLysAlaSerGlyAsnArgThrG 927

3087 CGCGTGGCGTTACCAACTCATCC.................GCAAAGACG 3118
          ::::::||||||:::|||                 |||||||||
 927 luValAsnAlaThrAsnAlaSerGlySerGlySerValThrAlaLysThr 943

3119 GCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAA 3168
     :::|||||||:::   |||      :::   |||              ||
 944 SerSerSerValAsnIleThrGlyAspLeuAsnThrIleAsnGlyLeuAs 960

3169 CTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAG 3218
     |         ::::::   :::|||      :::          ::::::
 960 nIleIleSerGluAsnGlyArgAsnThrValArgLeuArgGlyLysGluI 977

3219 CCTTGACGCGCTGATTGCGGCCGGGCGCGATGCCGCCGAAAAGACAGAAA 3268
          ::::::   ::::::|||||||:::  |||:::      :::|||:
 977 leGluValLysTyrIleGlnProGlyVal..AlaSer......ValGluG 991

3269 GCGTTGCCGAACCGGCCCGGCNGGCAGGCGGGGAAAATGTCGGCATTATG 3318
     ::|||   |||      |||          |||:::|||      :::
 991 luValIleGluAlaLysArgValLeu......GluLysValLysAspLeu 1005

3319 CAGGCGGAGGAAGAGAAA............................AA 3338
     :::   ||||||::::::                            ::
1006 SerAspGluGluArgGluThrLeuAlaLysLeuGlyValSerAlaValAr 1022

3339 ACGGGTGCAGGCGGATAAAGACAGCGCNTTGGCGAAACAGCGCGAAGCGG 3388
     :   ::::::   ::::::      ::::::      |||:::|||
1022 gPheIleGluProAsnAsnThrIleThrValAsnThrGlnAsnGluPheT 1039

3389 AAACCCGGCCGGNTACC 3405
       |||||||||::::::
1039 hrThrArgProSerSer 1044
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01836

seq_documentation_block:
ID   AAB01836 standard; Protein; 1079 AA.
XX
AC   AAB01836;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain LCDC2 HMW2A protein, SEQ ID NO:47.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain LCDC2.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52185.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 12; Fig 23A-P; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
XX
SQ   Sequence   1079 AA;

alignment_scores:
                Quality:  251.00              Length:   1090
                  Ratio:  0.485                 Gaps:     54
  Percent Similarity:  47.431    Percent Identity: 20.642

alignment_block:
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     772 GGCGACAGCGGTTCGCCAATGTTTATTTATGACAAAACAAACAATAAATG 821
         ||||||||||||      :::   :::|||   |||   :::|||:::
      80 GlyAspSerGlyHis...LeuThrLeuTyrLysLysArgLysAsnArg.. 94

     822 GCTGCTCAACGGAGTTTTACAAACCGGCTACCCTTATTCCGGCAGGGAAA 871
               :::      :::|||   :::          ::::::      :
      95 .......SerAspGlyIleGlnIleAsnLysAspIleThrSerThrGlyG 109

     872 ACGGTTTCCAGCTGATACGCAAAGATTGG......TTCTACGATGACATT 915
         ::::::::   :::         ||||||      ::::::   :::|||
     109 lySerLeuThrIleAsnSerAspAspTrpValAspIleHisGlyAsnIle 125

     916 TACAGAGGCGAT.....................ACACATACCGTCTNTTT 944
               |||:::                     :::   :::|||:::||
     126 ThrLeuGlyGluGlyPheLeuAsnIleThrSerSerAspSerValAlaPh 142

     945 TGAA......CCGCGCAGTAACGGACATTTTTCCTTTACATCCAACAACA 988
         ||||           ::::::|||:::   |||   :::::::::
     142 eGluGlyGlyAsnGlyAsnLysGlyArgSerSerAlaSerAlaGlnIleI 159

     989 ACGGTACGGGTACGGTAACAGAAACCAACGAAAAGGTNTCCAATCCAAAG 1038
           :::   ||||||:::|||   |||:::|||:::
     159 leAlaGlnGlyThrIleThrLeuThrGlyGluAsn.............. 170

    1039 CTTAAAGTACAGACAGTCCGACTGTTTGACGAATCTTTGAATGAAACTGA 1088
               :::|||   ||||||   :::   |||||||||   |||
     171 .........LysThrPheArgLeuAsnAsnValSerLeuAsnGlyThr.. 183

    1089 TAAAGAACCAGTTTACGCGGCAGGGGGTGTTAATCAGTACCGTCCAAGGT 1138

     183 ..................................................... 183

    1139 TAAACAACGGTGAAAACCTTTCTTTTATCGATTACGGCAACGGCAAACTC 1188
                                              |||||||||
     184 .................................GlyAsnGlyLeuSer 188

    1189 ATCTTATCAAACAACATCAACCAAGGC.........GCGGGCGGTTTGTA 1229
         |||:::|||:::      |||   :::          |||   :::
     189 IleIleSerThrAlaSerAsnLeuSerHisArgLeuAspGlyGluIleAs 205

    1230 TTTTGAAGGTGATTTTACGGTC.........TCGCCTGAAAACAACGAAA 1270
           :::|||:::   |||:::         :::   :::|||   |||
     205 nValSerGlyAsnValThrIleAsnGlnThrThrGlnGlnAsnIleGluT 222

    1271 CGTGGCAAGGC..................................... 1281
           |||::::::
     222 yrTrpLysAlaSerSerAspSerTyrTrpAsnValThrSerPheAsnLeu 238

    1281 ..................................................... 1281

     239 ArgGluAspSerLysPheThrPheIleLysTyrValAsnSerAlaArgAs 255

    1282 ........................GCGGGCGTT................. 1290
                                 |||||||||
     255 nGlyAspValArgGlyArgSerPheAlaGlyValIlePheAsnAlaLysG 272

    1291 ................CATATCAGTGAAGACAGTACCGTTACTTGGAAA 1323
                         ::::::::::::   |||||||||   :::|||
     272 lyLeuThrThrSerPheAsnValLysLysGlySerThrValAspPheLys 288

    1324 GTA......AACGGCGTGGCAAACGACCGC.................... 1347
         :::      |||:::      |||::::::
     289 LeuLysProAsnSerGlyTyrAsnSerGlnLysArgIleProIleGlnPh 305
```

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 845 rGluGlyThrAlaThrLeuThrAlaSer.............SerGlyL 857

2921 AATTGAAGCTGGCGGAAAGTTCCGAAGGNACT..... 2952
     |||||          ||||||:::   |||
 857 ysLeuThrThrGluAlaSerSerAsnIleThrSerAlaLysGlyGlnVal 873

2953 ..........................................TACAC 2957
                                                 ::
 874 AspLeuSerAlaGlnAspGlySerIleAlaGlyGlnIleSerAlaAlaAs 890

2958 CTTGGCGGTCAACAATACCGGCAACGAACCCGTAAGCCTCGATCAATTGA 3007
     ::::::::::|||:::||||||:::                  ||||
 890 nValThrLeuAsnThrThrGlyThr.................LeuT 900

3008 CGGTAGTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTC 3057
     ||:::||||||  |||::::::   |||          ||||||.:::
 900 hrThrValGlu.GlySerSerIleAsnAlaAsnGluGlyThrLeuValIl 916

3058 ACCCTGC.................AAAACGAACACGTCGATGCCGG 3086
         :::                 |||::::::   :::
 916 eAsnAlaAsnAspAlaLysLeuAspGlyLysAlaSerGlyAsnArgThrG 933

3087 CGCGTGGCGTTACCAACTCATCC.................GCAAAGACG 3118
         ::::::||||||:::|||                 |||||||||
 933 luValAsnAlaThrAsnAlaSerGlySerGlySerValThrAlaLysThr 949

3119 GCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAA 3168
     :::||||||:::   |||     :::   |||               ||
 950 SerSerSerValAsnIleThrGlyAspLeuAsnThrIleAsnGlyLeuAs 966

3169 CTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAG 3218
     |         ::::::   :::|||      :::         ::::::
 966 nIleIleSerGluAsnGlyArgAsnThrValArgLeuArgGlyLysGluI 983

3219 CCTTGACGCGCTGATTGCGGCCGGGCGCGATGCCGCCGAAAAGACAGAAA 3268
         ::::::   ::::::||||||:::  |||:::      :::|||:
 983 leGluValLysTyrIleGlnProGlyVal..AlaSer......ValGluG 997

3269 GCGTTGCCGAACCGGCCCGGCNGGCAGGCGGGGAAAATGTCGGCATTATG 3318
     ::|||   |||     |||           |||:::|||     :::
 997 luValIleGluAlaLysArgValLeu......GluLysValLysAspLeu 1011

3319 CAGGCGGAGGAAGAGAAA.............................AA 3338
     :::   ||||||::::::                            ::
1012 SerAspGluGluArgGluThrLeuAlaLysLeuGlyValSerAlaValAr 1028

3339 ACGGGTGCAGGCGGATAAAGACAGCGCNTTGGCGAAACAGCGCGAAGCGG 3388
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1028 gPheIleGluProAsnAsnThrIleThrValAsnThrGlnAsnGluPheT 1045

3389 AAACCCGGCCGGNTACC 3405
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1045 hrThrArgProSerSer 1050
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seq_documentation_block:
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XX
AC   AAR41731;
XX
DT   26-APR-1994  (first entry)
XX
DE   High molecular weight protein 3 (HMW3).
XX
KW   HMW; high molecular weight protein; virus; vaccine; influenza;
KW   epitope; immunity; haemophilus influenzae.
XX
OS   Haemophilus influenzae.
XX
PN   WO9319090-A.
XX
PD   30-SEP-1993.
XX
PF   16-MAR-1993;   93WO-US02166.
XX
PR   16-MAR-1992;   92GB-0005704.
XX
PA   (BARE/) BARENKAMP S J.
PA   (INRM ) INSERM INST NAT SANTE & RECH  MEDICALE.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1993-320683/40.
DR   N-PSDB; AAQ49510.
XX
PT   High molecular weight surface proteins - of non-typeable
PT   haemophilus which exhibit immunogenic properties
XX
PS   Claim 5; Figure 10; 100pp; English.
XX
CC   The isolation and purification of the high molecular weight protein
CC   enables the identification of the major protective epitopes of the
CC   protein by conventional epitope mapping.  These epitopes can then be
CC   synthesised using standard techniques and incorporated into fully
CC   synthetic or recombinant vaccines.
XX
SQ   Sequence   1338 AA;


alignment_scores:
           Quality:  251.00            Length:   1241
             Ratio:  0.418               Gaps:     69
 Percent Similarity:  48.429   Percent Identity: 21.515

alignment_block:
 US-09-303-518D-651 x AAR41731   ..

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      |||:::||||||:::|||                          :::::
   89 GlyGluThrTyrLeuGly.........................GlyAs 96

  177 AAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTNTACAACA 226
      :::::::|||:::       |||   :::  |||::::::   :::|
   96 pGluArgGlyGlu.........GlyLysAsnGlyIleGlnLeuAlaLysL 110

  227 AAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGAT 276
      ||                        ::::::   |||:::      |||:::
  110 ys..................ThrThrLeuGluLysGlySerThrIleAsn 120

  277 TTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAATA 326
         |||      :::::::::|||   |||   :::   ||||||
  121 ValSerGlyLysGluLysGlyGlyArgAlaIleValTrpGlyAspIleAl 137

  327 TATTGTG.........................AGCGTGGCACATAACG 349
       ::::::                       :::::::|||   :::|
  137 aLeuIleAspGlyAsnIleAsnAlaGlnGlyLysAspIleAlaLysThrG 154

  350 GCGGCTAT..................................... 357
      ||||||:::
  154 lyGlyPheValGluThrSerGlyHisTyrLeuSerIleAspAspAsnAla 170

  357 ..................................................... 357

  171 IleValLysThrLysGluTrpLeuLeuAspProGluAsnValThrIleGl 187

  358 ............AACAACGTTGATTTTGGTGCGGAAGGAAGNAATCCCG 394
                  ::::::|||::::::|||||                |
  187 uAlaProSerAlaSerArgValGluLeuGlyAla..............A 199

  395 ATCAGCACCGTTTTTCTTACCAAATTGTG.....AAAAGAAAT 432
      ||::::::      |||   :::::::::           |||:::|||
  199 spArgAsnSerHisSerAlaGluValIleLysValThrLeuLysLysAsn 215
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 735 GlyAsnLeuThrIleSerSerAspLysValAsnIleThrAsnGln..... 749

2007 CNACCGCACGTTTAAAGCGGAAAATTTCCATATTCAGGGCGGGCAGGCG. 2055
          |||:::||||||            :::::::||||||::::::
 750 ....IleThrIleLysAla.........GlyValGluGlyGlyArgSerA 762

2056 ............................GTGATTTCCCGCAATGTTGCC 2076
                                 :::|||:::   :::
 762 spSerSerGluAlaGluAsnAlaAsnLeuThrIleGlnThrLysGluLeu 778

2077 AAAGTGGAAGGCGATTGNCATTTGAGCAATCACGCCCAAGCAGTTTTTGG 2126
     |||:::   ||||||   ::::::|||:::      :::|||   :::
 779 LysLeuAlaGlyAspLeuAsnIleSerGlyPheAsnLysAlaGluIleTh 795

2127 TGTCGCACCGCATCAAAGCCATACAATCTGTACACGTTCGGACTGGACNG 2176
      :::         ::::::   ||||||   :::   |||
 795 rAlaLysAsnGlySerAspLeuThrIleGlyAsnAlaSerGly....... 809

2177 GTCTGACAAATTGTGTCGAANAAANCATTACCGACGATAAAGTGATTGCT 2226
           |||:::              :::|||   |||||||||
 810 .....GlyAsnAlaAspAlaLysLysValThrPheAspLysValLysAsp 824

2227 TCATTGACTAAGACNGACNTNAGCGGCANTGTNAGNCTNNCCNATNACGN 2276
     |||      :::|||||      :::         ::::::     ::
 825 SerLysIleSerThrAspGlyHisAsn.........ValThrLeuAsnSe 838

2277 TNNTTNAAANCTCNCNGGGCNTGCNNCACTNAANGGCAATCTTAGTGCAA 2326
     :           ::::::   ::::::   :::||||||   :::::::
 838 rGluValLysThrSerAsnGlySerSerAsnAlaGlyAsnAspAsnSerT 855

2327 ATGGCGATACA............CGTTATACAGTCAGCCACAACGCCACC 2364
     ::|||   |||                |||||||:::::|||:::|||
 855 hrGlyLeuThrIleSerAlaLysAspValThrValAsnAsnAsnValThr 871

2365 CAAAAC..........................GGCAACCTT........ 2379
     ::::::                         ||||||:::
 872 SerHisLysThrIleAsnIleSerAlaAlaAlaGlyAsnValThrThrLy 888

2380 ...................AGCCTCGTGGGCAATGCCCAAGCAACATTTA 2410
                        :::   :::|||:::::::::::|||   :
 888 sGluGlyThrThrIleAsnAlaThrThrGlySerValGluValThrAlaG 905

2411 ATCAAGCCACATTAAACGGCAACNCATCGGNTTCGGGCAATGCTTCATTT 2460
     :::::::::|||::::::||||||   :::                |||
 905 lnAsnGlyThrIleLysGlyAsnIleThr..............SerGln 916

2461 AATCTAAGCAACAACGCCGCACAAAACGGCAGTCTGACGCTTTCCGACAA 2510
     |||::::::   :::|||:::::::|||      |||:::   :::::::||
 917 AsnValThrValThrAlaThrGluAsn......LeuValThrThrGluAs 931

2511 CGCTAAGGCAAACGTAAGCCATTCCGCACTCAACGGCAATGTCTCCCTAG 2560
     ||||      |||            |||   :::|||:::|||:::::::
 931 nAlaValIleAsn............AlaThrSerGlyThrValAsnIleS 944

2561 CCGATAAGGCAGTATTCCATTTTGAAAACAGCCGCTTTACCGGACAACTC 2610
     ::   |||                                ||||||::::::
 944 erThrLys............................ThrGlyAspIle 950

2611 AGCGGC.........AGCAAGGANACAGCATTACACTTAAAAGACAGCGA 2651
     :::|||         |||   :::      :::::::::      |||
 951 LysGlyGlyIleGluSerThrSerGlyAsnValAsnIleThrAlaSerGl 967

2652 ATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTGACAACG 2701
         ||||||            :::::::::|||::::::   :::::::
 967 yAsnThrLeu............LysValSerAsnIleThrGlyGlnAspV 980

2702 CCACCATTACACTCAATTCCGCCTATCGCCACGATGCTGCAGGCGCG... 2748
     ::|||:::|||   :::::::::            :::|||||||:::
 980 alThrValThrAlaAspAlaGlyAlaLeuThrThrThrAlaGlySerThr 996

2749 ................................CAAACCGGCAGNGT 2762
                                     :::|||||||   ::
 997 IleSerAlaThrThrGlyAsnAlaAsnIleThrThrLysThrGlyAspIl 1013

2763 GTCAGACACGCCGCGCCGCCGTTCGCGCCGTTCCCTATTATCCGTTACAC 2812
     ::::          :::      |||          |||   :::|||
1013 eAsnGlyLysValGluSerSerSerGlySerValThrLeuValAlaThrG 1030

2813 CGCCAACTTCGGTAGAATCCCGTTTC......AACACGCTGACGGTA... 2853
          |||   :::   :::::::::      ||||||:::|||:::
1030 lyAlaThrLeuAlaValGlyAsnIleSerGlyAsnThrValThrIleThr 1046

2854 ......AACGGCAAATTGAACNGTCAAGGAACATTCCGCTTTATGTCGGA 2897
           :::|||||||||            |||             |||
1047 AlaAspSerGlyLysLeu............ThrSerThrValGlySerTh 1059

2898 ACTCTTCGGCTACCGAAGCGACAAATTGAAGCTGGCGGAAAGTTCC.... 2943
      :::   |||   :::|||             ::::::   ||||||
1059 rIleAsnGlyThrAsnSer............ValThrThrSerSerGlnS 1072

2944 ...........GAAGGNACTTACACCTTGGCGGTCAACAATACCGGCAAC 2982
                 |||||||||   :::         :::||||||   |||
1072 erGlyAspIleGluGlyThrIleSer.........GlyAsnThrValAsn 1085

2983 GAACCCGTAAGCCTCGATCAATTGACGGTA..............GTGGA 3017
          :::|||      :::|||||||:::               |||||
1086 ValThrAlaSerThrGlyAspLeuThrIleGlyAsnSerAlaLysValGl 1102

3018 AGGGAAAGACAACAAACCG......CTGTCCGAAAACCTTAATTTCACCC 3061
     |:::|||::::::              :::|||:::   :::::::|||
1102 uAlaLysAsnGlyAlaAlaThrLeuThrAlaGluSerGlyLysLeuThrT 1119

3062 TGCAAAACGAACACGTCGATG...CCGGCGCGTGGCGTTACCAACTCATC 3108
       ||| |||:::::::|||:::      ::::::|||   |||:::   ::
1119 hrGln.ThrGlySerSerIleThrSerSerAsnGlyGlnThrThrLeuTh 1135

3109 CGCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCT 3158
     :||||||   :::|||   |||      |||::::::   |||   ::::
1135 rAlaLysAspSerSerIleAlaGlyAsnIleAsnAlaAlaAsnValThrL 1152

3159 TTCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACA 3208
     ::   |||:::::::::              :::   :::   ::::::
1152 euAsnThrThrGlyThrLeuThrThrThrGlyAspSerLysIleAsnAla 1168

3209 ACGCGCAAAGCCTTGACG 3226
     |||      :::||||||
1169 ThrSerGlyThrLeuThr 1174
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1993.DAT:AAR41728

seq_documentation_block:

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ID   AAR41728 standard; Protein; 1477 AA.
XX
AC   AAR41728;
XX
DT   26-APR-1994  (first entry)
XX
DE   High molecular weight protein 2 (HMW2).
XX
KW   HMW; high molecular weight protein; virus; vaccine; influenza;
KW   epitope; immunity; haemophilus influenzae; gene cluster.
XX
OS   Haemophilus influenzae.
XX
PN   WO9319090-A.
XX
PD   30-SEP-1993.
XX
PF   16-MAR-1993;   93WO-US02166.
XX
PR   16-MAR-1992;   92GB-0005704.
XX
PA   (BARE/) BARENKAMP S J.
PA   (INRM ) INSERM INST NAT SANTE & RECH MEDICALE.
XX
PI   Barenkamp SJ;
```

```
XX
DR   WPI; 1993-320683/40.
DR   N-PSDB; AAQ49509.
XX
PT   High molecular weight surface proteins - of non-typeable
PT   haemophilus which exhibit immunogenic properties
XX
PS   Claim 4; Figure 4; 100pp; English.
XX
CC   The isolation and purification of the high molecular weight protein
CC   enables the identification of the major protective epitopes of the
CC   protein by conventional epitope mapping.  These epitopes can then be
CC   synthesised using standard techniques and incorporated into fully
CC   synthetic or recombinant vaccines.  This sequence is claimed to be
CC   the same as that given in AAR41724 (High molecular weight protein 2)
CC   although it does differ slightly.
XX
SQ   Sequence   1477 AA;
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alignment_scores:
           Quality:  251.00            Length:   1450
             Ratio:  0.382               Gaps:     67
 Percent Similarity:  45.310   Percent Identity: 19.172

alignment_block:
 US-09-303-518D-651 x AAR41728   ..

 Align seg 1/1  to: AAR41728  from: 1  to: 1477

     163 CGCGACTTTGCCGAAAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATAT 212
         :::|||          |||   :::   |||:::::::::::::   |||||
     158 LysAspAlaIleIleAsnThrAsnGlyPheThrAlaSerThrLeuAspIl 174

     213 TGAGGTNTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAA. 261
         |:::      |||   |||::::::            ::::::|||||
     174 eSerAsnGluAsnIleLysAlaArgAsnPheThrPheGluGlnThrLysA 191

     262 ..........GCCCCGATGATTGATTTTTCTGTG......GTGTCGCGT 294
                 |||   :::::::::   ::::::      |||:::::::
     191 spLysAlaLeuAlaGluIleValAsnHisGlyLeuIleThrValGlyLys 207

     295 AACGGCGTGGCGGCATTGGTGGGC............GATCAATATATTGT 332
         :::|||   :::   |||:::|||            ::::::   :::::
     208 AspGlySerValAsnLeuIleGlyGlyLysValLysAsnGluGlyValIl 224

     333 GAGCGTGGCACATAACGGCGGCTATAACAACGTTGATTTTGGT....... 375
         :||||||      |||||||||      ::::::      |||
     224 eSerVal......AsnGlyGlySerIleSerLeuLeuAlaGlyGlnLysI 239

     376 ........GCGGAAGGAAGNAATCCCGATCAGCACCGTTTTTCTTACCAA 417
                 ::::::      ||||||           :::::::|||:::
     239 leThrIleSerAspIleIleAsnPro.........ThrIleThrTyrSer 252

     418 ATTGTGAAAAGAAATAATTATAAGCCTGACAATTCACACCCTTACAACGG 467
         |||:::                  |||:::|||:::            ||
     253 IleAla..............AlaProGluAsnGluAlaValAsnLeuGl 264

     468 CGAT.................................TANCATATGC 481
         ||||                              :::   :::
     264 yAspIlePheAlaLysGlyGlyAsnIleAsnValArgAlaAlaThrIleA 281

     482 CGCGTTTGCATAAATTTGTCACAGATGCAGAACCTGTCGAAATGACGAGT 531
           :::      |||:::   :::|||:::           :::::::::
     281 rgAsnGlnGlyLysLeuSerAlaAspSer............ValSerLys 293

     532 GACATGAGGGGGAAT...ACCTATTCCGATAAAGAAAAATATCCCGAGCG 578
         |||      ||||||   :::   |||   ||||||         |||
     294 AspLysSerGlyAsnIleValLeuSerAlaLysGluGlyGluAlaGluIl 310

     579 TGTCCGCATCGGCTCAGGACACCACTATTGGCGTTATGATGATGACAAAC 628
               :::   |||:::::::::           ::::::   |||
     310 eGlyGlyValIleSerAlaGlnAsn............GlnGlnAlaLysG 323

     629 ACGGCGATTTATCCTACTCCGGCGCATGGTTAATT.............. 663
           |||   |||      :::|||      :::
     323 lyGlyLysLeuMetIleThrGlyAspLysValThrLeuLysThrGlyAla 339

     664 .......................GGCGGCAATACACATATG........ 681
                                 ||||||:::|||::::::
     340 ValIleAspLeuSerGlyLysGluGlyGlyGluThrTyrLeuGlyGlyAs 356

     682 ....CAGGGTTGGGGAAATAATGGCGTA..................... 705
             :::|||   |||:::||||||:::
     356 pGluArgGlyGluGlyLysAsnGlyIleGlnLeuAlaLysLysThrSerL 373

     706 ................NTTAGTTTGAGCGGCGATGTGCGC......CAT 732
                         ::::::||||||      :::      :::
     373 euGluLysGlySerThrIleAsnValSerGlyLysGluLysGlyGlyArg 389

     733 GCCAACGACTATGGCCCTATGCCGATT.................GCAGG 764
         |||      :::|||   :::   :::                  |||
     390 AlaIleValTrpGlyAspIleAlaLeuIleAspGlyAsnIleAsnAlaGl 406

     765 TGCGGCAGGCGACAGCGGTTCGCCAATGTTTATTTATGACAAAACAAACA 814
          ::::::||||||   :::                    ||||||
     406 nGlySerGlyAspIleAla.....................LysThr.... 414

     815 ATAAATGGCTGCTCAACGGAGTTTTACAAACCGGCTACCCTTATTCCGGC 864
                    :::|||   ::::::|||:::      |||   :::
     415 ..............GlyGlyPheValGluThrSerGlyHisTyrLeuSer 426

     865 AGGGAAAACGGTTTCCAGCTGATACGCAAAGATTGGTTCTACGAT..... 909
           :::::::::      :::      |||:::|||:::   |||
     427 IleAspSerAsnAlaIleValLysThrLysGluTrpLeuLeuAspProAs 443

     910 ......................GACATTTACAGAGGCGATACACATACCG 937
                                |||      |||::::::|||
     443 pAspValThrIleGluAlaGluAspProLeuArgAsnAsnThrGlyIleA 460

     938 TCTNTTTTGAACCGCGCAGTAACGGACATTTTTCCTTTACATCCAACAAC 987
                   |||   ::::::|||:::   |||      :::::::|||
     460 snAspGluPheProThrGlyThrGlyGluAlaSerAspProLysLysAsn 476

     988 AACGGTACGGGTACGGTAACAGAAACCAACGAAAAGGTNTCCAATCCAAA 1037
         :::          |||   |||   ||||||      :::||||||
     477 SerGluLeuLysThr...ThrLeuThrAsnThrThrIleSerAsnTyrLe 492

    1038 GCTTAAAGTACAGACAGTCCGACTGTTTGACGAATCTTTGAATGAAACTG 1087
           ::::::   |||:::                  :::::::::   :::
     492 uLysAsnAlaTrpThrMet..............AsnIleThrAlaSerA 504

    1088 ATAAAGAACCAGTTTACGCGGCAGGGGGTGTTAATCAGTACCGTCCAAGG 1137
           |||      |||   ::::::
     504 rgLysLeuThrValAsnSerSer........................... 511

    1138 TTAAACAACGGTGAAAACCTTTCTTTTATCGATTACGGCAACGGCAAACT 1187
         :::|||   |||:::|||      :::|||   ::::::::::|||
     512 IleAsnIleGlySerAsnSerHisLeuIleLeuHisSerLysGly..... 526

    1188 CATCTTATCAAACAACATCAACCAAGGCGCGGGCGGTTTGTATTTTGAAG 1237
                              |||   :::|||||||:::   ::::::|
     527 .....................GlnArgGlyGlyGlyValGlnIleAspG 536

    1238 GTGATTTTACGGTCTCGCCTGAAAACAACGAAACGTGGCAAGGCGCGGGC 1287
         |||||:::|||   :::      |||         :::::::|||:::
     536 lyAspIleThrSerLysGlyGlyAsnLeuThrIleTyrSerGlyGlyTrp 552

    1288 GTTCATATCAGTGAAGACAGTACCGTTACTTGGAAAGTAAACGGCGTGGC 1337
         |||   :::   ::::::   |||:::
     553 ValAspValHisLysAsnIleThrLeu....................... 561

    1338 AAACGACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCA 1387

     561 ..................................................... 561
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1388 AAGGGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTG 1437
              :::||||||  :::::::::    ::::::|||  :::
 562 ........AspGlnGlyPheLeuAsnIleThrAlaAlaSerValAlaPhe 575

1438 GATCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGG 1487
       :::   ::::::::|||:::::     |||   ::::::|||
 576 ...GluGlyGlyAsnAsnLysAlaArgAspAlaAlaAsnAlaLysIle.. 590

1488 CTTGNTCAGCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCA 1537
                :::::||||||||  :::::::::::::::::
 591 .......ValAlaGlnGlyThrValThrIleThrGlyGluGlyLys.... 603

1538 ACCCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAAC 1587
                         ||||||:::::::::::::::||||||
 604 ...................AspPheArgAlaAsnAsnValSerLeuAsn 613

1588 GGGCATTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGAT 1637
     |||   :::   :::::::::   |||::::::::::::::
 614 GlyThrGlyLysGlyLeuAsnIleIleSerSerValAsnAsn........ 627

1638 GATTGNCNATCATAATGCCACAACAACATCCACCGTTACCATTACAGGGA 1687
           ::|||||||           ::::::|||::::::|||::||||
 628 ....LeuThrHisAsn......LeuSerGlyThrIleAsnIleSerGlyA 641

1688 ATGAAAGTATTACACAACCGAGTGGTAAG..................... 1716
     ||   :::|||:::|||   :::   |||
 641 snIleThrIleAsnGlnThrThrArgLysAsnThrSerTyrTrpGlnThr 657

1717 ..................AATATCAATAGACTTAATTACAGCAAAGAAAT 1748
                       |||:::::   ||||||       |||
 658 SerHisAspSerHisTrpAsnValSerAlaLeuAsnLeu......GluTh 672

1749 TGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGC 1798
       :::   |||      |||   :::       :::::::::::::::|||
 672 rGlyAlaAsnPheThrPheIleLysTyrIleSerSerAsnSerLysGly. 688

1799 GGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCNGCTGCTT 1848
        |||:::      |||:::   :::|||
 689 ..LeuThrThrGlnTyrArgSerSerAla..................... 697

1849 TCCGGCGGAACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACT 1898
           |||:::|||:::||||||           :::||||||:::::
 698 ......GlyValAsnPheAsnGly...........ValAsnGlyAsnMe 708

1899 GTTTTTC........................................... 1905
     :  |||
 708 tSerPheAsnLeuLysGluGlyAlaLysValAsnPheLysLeuLysProA 725

1906 ..............AGCGGCAGACCGACACCGCACGCCTAC......... 1932
                    :::::::::|||   |||      :::
 725 snGluAsnMetAsnThrSerLysProLeuProIleArgPheLeuAlaAsn 741

1933 ..............................................AATCA 1937
                                                  |||||
 742 IleThrAlaThrGlyGlyGlySerValPhePheAspIleTyrAlaAsnHi 758

1938 TTTAGGAAGCGGGTGGTCAAAAATGGAAGGTATCCCACAAGGAGAAATCG 1987
     |   |||  |||                   :::   ::::::||||||
 758 sSerGlyArgGly...........AlaGluLeuLysMetSerGluIleA 771

1988 TGTGGGACAACGACTGGATCNACCGCACGTTTAAAGCGGAAAATTTC... 2034
        :::|||                        :::   ||||||
 771 snIleSerAsn.......................GlyAlaAsnPheThr 779

2035 .........CATATTCAGGGCGGGCAGGCGGTGATTTCCCGCAATGTTGC 2075
               |||:::::|||   :::|||
 780 LeuAsnSerHisValArgGlyAspAspAlaPhe................ 790

2076 CAAAGTGGAAGGCGATTGNCATTTGAGCAATCACGCCCAAGCAGTTTTTG 2125
      |||:::::   |||     :::::
 791 .LysIleAsnLysAspLeuThrIleAsn..................... 799

2126 GTGTCGCACCGCATCAAAGCCATACAATCTGTACACGTTCGGACTGGACN 2175

                                  :::|||:::|||::::::
 800 ...........................AlaThrAsnSerAsnPhe... 805

2176 GGTCTGACAAATTGTGTCGAANAAANCATTACCGACGATAAAGTGATTGC 2225

 805 .................................................. 805

2226 TTCATTGACTAAGACNGACNTNAGCGGCANTGTNAGNCTNNCCNATNACG 2275
      ||||||   :::|||       :::                :::    :
 806 .SerLeuArgGlnThrLysAspAspPheTyrAspGlyTyrAlaArgAsnA 822

2276 NTNNTTNAAANCTCNCNGGGCNTGCNNCACTNAANGGCAATCTTAGTGCA 2325
     ::      :::     :::   :::   |||   ||||||::::::
 822 laIleAsnSerThrTyrAsnIleSerIleLeuGlyGlyAsnValThrLeu 838

2326 AATGGCGATACACGTTATACAGTCAGCCACAACGCCACCCAAAACGGCAA 2375
     :::|||                              ||||||::::::
 839 GlyGly..............................GlnAsnSerSe 844

2376 CCTTAGCCTCGTGGGCAATGCCCAAGCAACATTTAATCAAGCC....... 2418
     :   |||:::::||||||          |||::::::::::|||
 844 rSerSerIleThrGlyAsn......IleThrIleGluLysAlaAlaAsnV 859

2419 ..ACATTAAACGGCAACNCATCGGNTTCGGGCAATGCTTCATTTAATCTA 2466
       ||||||::::::|||   :::   :::   :::          |||:::
 859 alThrLeuGluAlaAsnAsnAlaProAsnGlnGln.........AsnIle 872

2467 AGCAACAACGCCGCACAAAACGGCAGTCTGACGCTTTCCGACAACGCTAA 2516
       :::::::::   :::   |||||||||   ::::::   :::   ::
 873 ArgAspArgValIleLysLeuGlySerLeuLeuValAsnGlySerLeuSe 889

2517 GGCAAACGTAAGCCATTCCGCACTCAACGGCAATGTCTCCCTAGCCGATA 2566
     :   :::   :::::::::   ::::::||||||:::::::::::::::
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2567 AGGCAGTATTCCAT.........TTTGAAAACAGCCGCTTTACCGGACAA 2607
     :::|||:::|||              ::::::   ::::::||||||:::
 906 erAlaThrPheLysGlyLysThrArgAspThrLeuAsnIleThrGlyAsn 922

2608 CTCAGCGGCAGCAAGGANACAGCATTACACTTAAAAGACAGCGAATGGAC 2657
     ::::::::::::   ::::::   :::::::::   ::::::
 923 PheThrAsnAsnGlyThrAlaGluIleAsnIleThrGlnGlyValValLy 939

2658 GCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTGACAACGCCACCA 2707
       |||   :::   |||:::   |||:::|||||||:::
 939 sLeuGlyAsnValThrAsnAspGlyAspLeuAsnIle............ 951

2708 TTACACTCAATTCCGCCTATCGCCACGATGCTGCAGGCGCGCAAACCGGC 2757

 951 .................................................. 951

2758 AGNGTGTCAGACACGCCGCGCCGCCGTTCGCGCCGTTCCCTATTATCCGT 2807
                  |||         :::|||::::::||||||:::::::::
 952 .........ThrThrHisAlaLysArgAsnGlnArgSerIleIleGly.. 964

2808 TACACCGCCAACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACG 2857
                                 :::   ::::::   :::|
 965 ...........................GlyAspIleIleAsnLysLysG 972

2858 GCAAATTGAACNGTCAAGGAACATTCCGCTTTATGTCG...GAACTCTTC 2904
      ||:::||||||         :::   :::      :::   ::::::
 972 lySerLeuAsnIleThrAspSerAsnAsnAspAlaGluIleGlnIleGly 988

2905 GGCTACCGAAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGNACTTA 2954
      |||      |||:::|||                    ||||||:::
 989 GlyAsnIleSerGlnLys.....................GluGlyAsnLe 998

2955 CACCTTGGCG.........GTCAACAATACCGGCAACGAACCCGTAAGCC 2995
      |||::::::           :::|||   |||
 998 uThrIleSerSerAspLysIleAsnIleThr.................. 1008

2996 TCGATCAATTGACGGTAGTGGAAGGGAAAGACAACAAACCGCTGTCC... 3042
        |||:::|||:::   :::|||   |||::::::      |||
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1009 ..LysGlnIleThrIleLysLysGlyIleAspGlyGluAspSerSerSer 1024

3043 .........GAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGATGC 3083
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1025 AspAlaThrSerAsnAlaAsnLeuThrIleLys..................... 1035

3084 CGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGC 3133

1035 ..................................................... 1035

3134 ATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACTC............. 3171
           :::||||||   :::|||::::::   |||
1036 ........ThrLysGluLeuLysLeuThrGluAspLeuSerIleSerGly 1049

3172 ...GGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAG 3218
      :::|||||||||           :::   ||||||
1050 PheAsnLysAlaGluIle.........ThrAlaLysAsp............ 1059

3219 CCTTGACGCGCTGATTGCGGCCGGGCGCGATGCCGCCGAAAAGACAGAAA 3268
                            |||||||||
1060 .....................GlyArgAspLeu................. 1063

3269 GCGTTGCCGAACCGGCCCGGCNGGCAGGCGGGGAAAATGTCGGCATTATG 3318
                       :::   |||::::::|||   |||
1064 ...................ThrIleGlyAsnSerAsnAspGlyAsnSer 1073

3319 CAGGCGGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACAGCGCNTT 3368
      ||||||   :::          :::      |||||||||   ::
1074 GlyAlaGluAlaLysThrValThrPheAsnAsnValLysAspSerLysIl 1090

3369 GGCGAAACAGCGCGAAGCGGAAACC.........CGGCCGGNTACCACCG 3409
     ::::   :::   :::      |||         :::      |||::::
1090 eSerAlaAspGlyHisAsnValThrLeuAsnSerLysValLysThrSerS 1107

3410 CCTTCCCCCGCGCCCGCNGCGCCCGCCGGGATTTGCCGCAACCGCAGCCC 3459
     ::         :::|||   ::::::   |||
1107 erSerAsnGlyGlyArgGluSerAsnSerAspAsnAspThrGlyLeuThr 1123

3460 CAACCGCAACCTCAACCCCAACCGCAGCGCGACCTGATNAGC...CGTTA 3506
                :::   :::   ::::::|||::::::|||   :::
1124 IleThrAlaLysAsnValGluValAsnLysAspIleThrSerLeuLysTh 1140

3507 TGCCAATAGCGGTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTTTTCG 3556
      :::|||         ||||||      :::||| :::::::::   :::
1140 rValAsnIleThrAlaSerGluLysValThrThr.ThrAlaGlySerThr 1156

3557 CCGTACAGGACGAATTGGACCGCGTGTTTGCCGAAGACCGCCGCAACGCN 3606
           ||||||      |||   :::         ::::::
1157 IleAsnAlaThrAsnGlyLysAlaSerIleThrThrLysThrGlyAspIl 1173

3607 GTTTGGACAAGCNGCATCCGGNACACCAAACACTACCGTTCGC...AAGA 3653
       |||      :::::::::|||   ::::::::::::         :
1173 eSerGlyThrIleSerGlyAsnThrValSerValSerAlaThrGlyAspL 1190

3654 TTTCCGCGCCTACCGCCAACAAACCGACCTGCGCCAAATCGGTATGCAGA 3703
     ::::::::   ::::::::::|||      :::   ::::::   ::::::
1190 euThrThrLysSerGlySerLysIleGluAlaLysSerGlyGluAlaAsn 1206

3704 AAAACCTCGGCAGCGGGCGCGTCGGCATCCTGTTTTCGCACAACCGGACC 3753
        |||||||||:::|||:::   ::::::         |||   :::
1207 ValThrSerAlaThrGlyThrIleGlyGly.........ThrIleSerGl 1220

3754 GAAAACANCTTCGACGACGGCATCGGCA..................... 3781
      :::|||   ::::::||||||:::|||
1220 yAsnThrValAsnValThrAlaAsnAlaGlyAspLeuThrValGlyAsnG 1237

3782 ..............ACTCGGCACGGCTTGCCCACGGCGCCCGTTTTCGGGC 3817
                    :::   :::|||      |||         :::|||
1237 lyAlaGluIleAsnAlaThrGluGlyAlaAlaThrLeuThrAlaThrGly 1253

3818 AAT......ACGGCATCGGCAGGTTCGACATCGGCATCAGCACGGGCGCG 3861
     |||      |||::::::||||||||||:::   :::|||:::::::::::
1254 AsnThrLeuThrThrGluAlaGlySerSerIleThrSerThrLysGlyGl 1270

3862 GGTTTTAGCAGCGGCANTCTNTCAGACGGCATCGGAGGCAAAATCCGCCG 3911
      :|||         |||      |||::::::|||   |||   |||
1270 nValAspLeuLeuAla......GlnAsnGlySerIleAlaGlySerIleA 1285

3912 CCGCGTGCTGCATTACGGCATTCAGGCACGATACCGCGCCGGTTTCGGCG 3961
       |||:::   :::|||               |||      :::   |||
1285 snAlaAlaAsnValThrLeuAsnThrThrGlyThrLeuThrThrValAla 1301

3962 GATTCGGCATCGAACCGTACATCGGCGCAACGCGCTATTTCGTCCAAA 4009
       |||      :::   ||||||:::      :::|||::::::|||
1302 GlySerAspIleLysAlaThrSerGlyThrLeuValIleAsnAlaLys 1317
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seq_documentation_block:

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ID   AAR63506 standard; Protein; 1477 AA.
XX
AC   AAR63506;
XX
DT   25-JUN-1995  (first entry)
XX
DE   Haemophilus high molecular weight protein HMW2.
XX
KW   High molecular weight protein; HMW2; protective vaccine; otitis;
KW   sinusitis; bronchitis; Hib; ss.
XX
OS   Haemophilus.
XX
PN   WO9421290-A.
XX
PD   29-SEP-1994.
XX
PF   15-MAR-1994;   94WO-US02550.
XX
PR   16-MAR-1993;   93US-0038682.
XX
PA   (BARE/) BARENKAMP S J.
PA   (SGEM/) ST GEME J W.
XX
PI   Barenkamp SJ,  St GEME JW;
XX
DR   WPI; 1994-316665/39.
DR   Q-PSDB; Q72294.
XX
PT   New immunogenic high mol. wt. proteins of non typeable
PT   Haemophilus - useful in protective vaccines
XX
PS    Claim 3; Page 36; 127pp; English.
XX
CC   The HMW2 protein encoded by this sequence is useful in a vaccine to
CC   protect against disease caused by non-typeable Haemophilus which are
CC   not controlled by H. influenzae type b (Hib) vaccines.  The encoded
CC   protein can also be used as a carrier for protective Hib
CC   polysaccharide (in a conjugate vaccin against meningitis) or for
CC   other antigens, haptens, etc.
XX
SQ   Sequence   1477 AA;
```

```
alignment_scores:
            Quality:  251.00              Length:   1447
              Ratio:  0.380                 Gaps:     65
 Percent Similarity:  45.612   Percent Identity: 19.143

alignment_block:
 US-09-303-518D-651 x AAR63506   ..

 Align seg 1/1  to: AAR63506  from: 1  to: 1477

     163 CGCGACTTTGCCGAAAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATAT 212
           :::|||         |||   :::   |||::::::::::::   |||||
     158 LysAspAlaIleIleAsnThrAsnGlyPheThrAlaSerThrLeuAspIl 174
```

```
213 TGAGGTNTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAA. 261
    |:::      |||   |||::::::           ::::::|||||| 
174 eSerAsnGluAsnIleLysAlaArgAsnPheThrPheGluGlnThrLysA 191

262 ..........GCCCCGATGATTGATTTTTCTGTG......GTGTCGCGT 294
            |||   :::::::::   ::::::      |||::::::: 
191 spLysAlaLeuAlaGluIleValAsnHisGlyLeuIleThrValGlyLys 207

295 AACGGCGTGGCGGCATTGGTGGGC...........GATCAATATATTGT 332
    :::|||   :::   |||:::|||           ::::::   ::::: 
208 AspGlySerValAsnLeuIleGlyGlyLysValLysAsnGluGlyValIl 224

333 GAGCGTGGCACATAACGGCGGCTATAACAACGTTGATTTTGGT....... 375
    :||||||      |||||||||      ::::::      ||| 
224 eSerVal......AsnGlyGlySerIleSerLeuLeuAlaGlyGlnLysI 239

376 ........GCGGAAGGAAGNAATCCCGATCAGCACCGTTTTTCTTACCAA 417
            ::::::      ||||||           ::::::|||::: 
239 leThrIleSerAspIleIleAsnPro.........ThrIleThrTyrSer 252

418 ATTGTGAAAAGAAATAATTATAAGCCTGACAATTCACACCCTTACAACGG 467
    |||:::                |||:::|||:::           || 
253 IleAla..............AlaProGluAsnGluAlaValAsnLeuGl 264

468 CGAT.....................................TANCATATGC 481
    ||||                                   :::   ::: 
264 yAspIlePheAlaLysGlyGlyAsnIleAsnValArgAlaAlaThrIleA 281

482 CGCGTTTGCATAAATTTGTCACAGATGCAGAACCTGTCGAAATGACGAGT 531
      :::      |||:::   :::|||:::           :::::::: 
281 rgAsnGlnGlyLysLeuSerAlaAspSer............ValSerLys 293

532 GACATGAGGGGGAAT...ACCTATTCCGATAAAGAAAAATATCCCGAGCG 578
    |||      ||||||   :::   |||   ||||||        ||| 
294 AspLysSerGlyAsnIleValLeuSerAlaLysGluGlyGluAlaGluIl 310

579 TGTCCGCATCGGCTCAGGACACCACTATTGGCGTTATGATGATGACAAAC 628
          :::   |||:::::::::           ::::::   ||| 
310 eGlyGlyValIleSerAlaGlnAsn............GlnGlnAlaLysG 323

629 ACGGCGATTTATCCTACTCCGGCGCATGGTTAATT.............. 663
    |||   |||      :::|||      :::                  
323 lyGlyLysLeuMetIleThrGlyAspLysValThrLeuLysThrGlyAla 339

664 .......................GGCGGCAATACACATATG........ 681
                            ||||||:::|||:::::: 
340 ValIleAspLeuSerGlyLysGluGlyGlyGluThrTyrLeuGlyGlyAs 356

682 ....CAGGGTTGGGGAAATAATGGCGTA..................... 705
        :::|||   |||:::|||||||::: 
356 pGluArgGlyGluGlyLysAsnGlyIleGlnLeuAlaLysLysThrSerL 373

706 ................NTTAGTTTGAGCGGCGATGTGCGC.....:.CAT 732
                    ::::::|||||      :::      ::: 
373 euGluLysGlySerThrIleAsnValSerGlyLysGluLysGlyGlyArg 389

733 GCCAACGACTATGGCCCTATGCCGATT.................GCAGG 764
    |||      :::|||   :::   :::                  ||| 
390 AlaIleValTrpGlyAspIleAlaLeuIleAspGlyAsnIleAsnAlaGl 406

765 TGCGGCAGGCGACAGCGGTTCGCCAATGTTTATTTATGACAAAACAAACA 814
     ::::::|||||   :::                    |||||| 
406 nGlySerGlyAspIleAla.....................LysThr.... 414

815 ATAAATGGCTGCTCAACGGAGTTTTACAAACCGGCTACCCTTATTCCGGC 864
                  :::|||   ::::::|||:::      |||   ::: 
415 .............GlyGlyPheValGluThrSerGlyHisTyrLeuSer 426

865 AGGGAAAACGGTTTCCAGCTGATACGCAAAGATTGGTTCTACGAT..... 909
    :::::::::      :::      |||:::|||:::   ||| 
427 IleAspSerAsnAlaIleValLysThrLysGluTrpLeuLeuAspProAs 443

910 .....................GACATTTACAGAGGCGATACACATACCG 937
                           |||      |||::::::|||
443 pAspValThrIleGluAlaGluAspProLeuArgAsnAsnThrGlyIleA 460

938 TCTNTTTTGAACCGCGCAGTAACGGACATTTTTCCTTTACATCCAACAAC 987
                |||   ::::::|||:::   |||      :::::::||| 
460 snAspGluPheProThrGlyThrGlyGluAlaSerAspProLysLysAsn 476

988 AACGGTACGGGTACGGTAACAGAAACCAACGAAAAGGTNTCCAATCCAAA 1037
    :::          |||   |||   ||||||      :::|||||| 
477 SerGluLeuLysThr...ThrLeuThrAsnThrThrIleSerAsnTyrLe 492

1038 GCTTAAAGTACAGACAGTCCGACTGTTTGACGAATCTTTGAATGAAACTG 1087
       ::::::   |||                          ||||||   ||| 
492 uLysAsnAlaTrpThr.....................LeuAsnIleThrA 502

1088 ATAAAGAACCAGTTTACGCGGCAGGGGGTGTTAATCAGTACCGTCCAAGG 1137
     ::::::   :::                ||||||
502 laSerArgLysLeu.............ThrValAsn.............. 509

1138 TTAAACAACGGTGAAAACCTTTCTTTTATCGATTACGGCAACGGCAAACT 1187
                           |||   |||:::   |||:::::::::: 
510 .....................SerSerIleAsnIleGlySerAsnSerHi 519

1188 CATCTTATCAAACAACATCAACCAAGGCGCGGGCGGTTTGTATTTTGAAG 1237
     ::::::   ::::::   :::|||   :::|||||||:::   ::::::| 
519 sLeuIleLeuHisSerLysGlyGlnArgGlyGlyGlyValGlnIleAspG 536

1238 GTGATTTTACGGTCTCGCCTGAAAACAACGAAACGTGGCAAGGCGCGGGC 1287
     ||||||:::|||   :::      |||         ::::::|||::: 
536 lyAspIleThrSerLysGlyGlyAsnLeuThrIleTyrSerGlyGlyTrp 552

1288 GTTCATATCAGTGAAGACAGTACCGTTACTTGGAAAGTAAACGGCGTGGC 1337
     |||   :::   ::::::   |||::: 
553 ValAspValHisLysAsnIleThrLeu..................... 561

1338 AAACGACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCA 1387

561 ..................................................... 561

1388 AAGGGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTG 1437
           :::|||||||   :::::::::      ::::::|||   ::: 
562 ........AspGlnGlyPheLeuAsnIleThrAlaAlaSerValAlaPhe 575

1438 GATCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGG 1487
       :::   :::::::::|||::::::      |||   :::::::||| 
576 ...GluGlyGlyAsnAsnLysAlaArgAspAlaAlaAsnAlaLysIle.. 590

1488 CTTGNTCAGCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCA 1537
                ::::::|||||||||   :::::::::::::::::: 
591 .......ValAlaGlnGlyThrValThrIleThrGlyGluGlyLys.... 603

1538 ACCCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAAC 1587
                              ||||||:::::::::::::::||||||
604 ...................AspPheArgAlaAsnAsnValSerLeuAsn 613

1588 GGGCATTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGAT 1637
     |||   :::   :::::::::   |||:::::::::::::: 
614 GlyThrGlyLysGlyLeuAsnIleIleSerSerValAsnAsn........ 627

1638 GATTGNCNATCATAATGCCACAACAACATCCACCGTTACCATTACAGGGA 1687
           :::||||||         ::::::|||:::::::|||:::|||| 
628 ....LeuThrHisAsn......LeuSerGlyThrIleAsnIleSerGlyA 641

1688 ATGAAAGTATTACACAACCGAGTGGTAAG..................... 1716
     ||   :::|||:::|||   :::   |||
641 snIleThrIleAsnGlnThrThrArgLysAsnThrSerTyrTrpGlnThr 657

1717 .................AATATCAATAGACTTAATTACAGCAAAGAAAT 1748
                       |||::::::   ||||||         ||| 
658 SerHisAspSerHisTrpAsnValSerAlaLeuAsnLeu......GluTh 672

1749 TGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGC 1798
```

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 672 rGlyAlaAsnPheThrPheIleLysTyrIleSerSerAsnSerLysGly. 688

1799 GGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCNGCTGCTT 1848
689 ..LeuThrThrGlnTyrArgSerSerAla..................... 697

1849 TCCGGCGGAACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACT 1898
698 ......GlyValAsnPheAsnGly............ValAsnGlyAsnMe 708

1899 GTTTTTC..................................... 1905
708 tSerPheAsnLeuLysGluGlyAlaLysValAsnPheLysLeuLysProA 725

1906 .............AGCGGCAGACCGACACCGCACGCCTAC.......... 1932
725 snGluAsnMetAsnThrSerLysProLeuProIleArgPheLeuAlaAsn 741

1933 ..........................................AATCA 1937
742 IleThrAlaThrGlyGlyGlySerValPhePheAspIleTyrAlaAsnHi 758

1938 TTTAGGAAGCGGGTGGTCAAAAATGGAAGGTATCCCACAAGGAGAAATCG 1987
758 sSerGlyArgGly.............................. 762

1988 TGTGGGACAACGACTGGATCNACCGCACGTTTAAAGCGGAAAATTTCCAT 2037
763 ....................AlaGluLeuLysMetSerGluIleAsn 771

2038 ATTCAGGGCGGGCAGGCGGTGATTTCCCGCAATGTTGCCAAAGTGGAAGG 2087
772 IleSerAsnGly.................................Al 776

2088 CGATTGNCATTTGAGCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGC 2137
776 aAsnPheThrLeuAsnSerHisValArgAlaAspAspAlaPheLysIleA 793

2138 ATCAAAGCCATACAATC...TGTACACGTTCGGACTGGACNGGTCTGACA 2184
793 snLysAspLeuThrIleAsnAlaThrAsnSerAsnPhe..... 805

2185 AATTGTGTCGAANAAANCATTACCGACGATAAAGTGATTGCTTCATTGAC 2234
806 .....SerLeuAr 808

2235 TAAGACNGACNTNAGCGGCANTGTNAGNCTNNCCNATNACGNTNNTTNAA 2284
808 gGlnThrLysAspAspPheTyrAspGlyTyrAlaArgAsnAlaIleAsnS 825

2285 ANCTCNCNGGGCNTGCNNCACTNAANGGCAATCTTAGTGCAAATGGCGAT 2334
825 erThrTyrAsnIleSerIleLeuGlyGlyAsnValThrLeuGlyGly... 840

2335 ACACGTTATACAGTCAGCCACAACGCCACCCAAAACGGCAACCTTAGCCT 2384
841 .....GlnAsnSerSerSerSerIl 847

2385 CGTGGGCAATGCCCAAGCAACATTTAATCAAGCC.....ACATTAA 2425
847 eThrGlyAsn......IleThrIleGluLysAlaAlaAsnValThrLeuG 862

2426 ACGGCAACNCATCGGNTTCGGGCAATGCTTCATTTAATCTAAGCAACAAC 2475
862 luAlaAsnAsnAlaProAsnGlnGln.....AsnIleArgAspArg 875

2476 GCCGCACAAAACGGCAGTCTGACGCTTTCCGACAACGCTAAGGCAAACGT 2525
876 ValIleLysLeuGlySerLeuLeuValAsnGlySerLeuSerLeuThrGl 892

2526 AAGCCATTCCGCACTCAACGGCAATGTCTCCCTAGCCGATAAGGCAGTAT 2575
892 yGluAsnAlaAspIleLysGlyAsnLeuThrIleSerGluSerAlaThrP 909

2576 TCCAT.....TTTGAAAACAGCCGCTTTACCGGACAACTCAGCGGC 2616
909 heLysGlyLysThrArgAspThrLeuAsnIleThrGlyAsnPheThrAsn 925

2617 AGCAAGGANACAGCATTACACTTAAAAGACAGCGAATGGACGCTGCCGTC 2666
926 AsnGlyThrAlaGluIleAsnIleThrGlnGlyValValLysLeuGlyAs 942

2667 AGGCACGGAATTAGGCAATTTAAACCTTGACAACGCCACCATTACACTCA 2716
942 nValThrAsnAspGlyAspLeuAsnIle..................... 951

2717 ATTCCGCCTATCGCCACGATGCTGCAGGCGCGCAAACCGGCAGNGTGTCA 2766
951 ..................................................... 951

2767 GACACGCCGCGCCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCC 2816
952 ThrThrHisAlaLysArgAsnGlnArgSerIleIleGly........... 964

2817 AACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGA 2866
965 .................GlyAspIleIleAsnLysLysGlySerLeuA 975

2867 ACNGTCAAGGAACATTCCGCTTTATGTCG...GAACTCTTCGGCTACCGA 2913
975 snIleThrAspSerAsnAsnAspAlaGluIleGlnIleGlyGlyAsnIle 991

2914 AGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGNACTTACACCTTGGC 2963
992 SerGlnLys.....................GluGlyAsnLeuThrIleSe 1001

2964 G.........GTCAACAATACCGGCAACGAACCCGTAAGCCTCGATCAAT 3004
1001 rSerAspLysIleAsnIleThr.....................LysGlnI 1011

3005 TGACGGTAGTGGAAGGGAAAGACAACAAACCGCTGTCC..... 3042
1011 leThrIleLysLysGlyIleAspGlyGluAspSerSerSerAspAlaThr 1027

3043 GAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGATGCCGGCGCGTG 3092
1028 SerAsnAlaAsnLeuThrIleLys..... 1035

3093 GCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCGG 3142
1036 .....T 1036

3143 TCAAAGAACAAGAGCTTTCCGACAAACTC.....GGCAAG 3177
1036 hrLysGluLeuLysLeuThrGluAspLeuSerIleSerGlyPheAsnLys 1052

3178 GCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTGACGC 3227
1053 AlaGluIle.....ThrAlaLysAsp..... 1059

3228 GCTGATTGCGGCCGGGCGCGATGCCGCCGAAAAGACAGAAAGCGTTGCCG 3277
1060 .....GlyArgAspLeu..... 1063

3278 AACCGGCCCGGCNGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCGGAG 3327
1064 .....ThrIleGlyAsnSerAsnAspGlyAsnSerGlyAlaGlu 1076

3328 GAAGAGAAAAAACGGGTGCAGGCGGATAAAGACAGCGCNTTGGCGAAACA 3377
1077 AlaLysThrValThrPheAsnAsnValLysAspSerLysIleSerAlaAs 1093

3378 GCGCGAAGCGGAAACC.....CGGCCGGNTACCACCGCCTTCCCCC 3418
1093 pGlyHisAsnValThrLeuAsnSerLysValLysThrSerSerSerAsnG 1110
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3419 GCGCCCGCNGCGCCCGCCGGGATTTGCCGCAACCGCAGCCCCAACCGCAA 3468
     :::|||   ::::::   |||
1110 lyGlyArgGluSerAsnSerAspAsnAspThrGlyLeuThrIleThrAla 1126

3469 CCTCAACCCCAACCGCAGCGCGACCTGATNAGC...CGTTATGCCAATAG 3515
        :::   :::   ::::::|||:::::::|||   :::   :::|||
1127 LysAsnValGluValAsnLysAspIleThrSerLeuLysThrValAsnIl 1143

3516 CGGTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTTTTCGCCGTACAGG 3565
           ||||||      :::||| :::::::::   :::
1143 eThrAlaSerGluLysValThrThr.ThrAlaGlySerThrIleAsnAla 1159

3566 ACGAATTGGACCGCGTGTTTGCCGAAGACCGCCGCAACGCNGTTTGGACA 3615
     ||||||     |||   :::         ::::::         |||
1160 ThrAsnGlyLysAlaSerIleThrThrLysThrGlyAspIleSerGlyTh 1176

3616 AGCNGCATCCGGNACACCAAACACTACCGTTCGC...AAGATTTCCGCGC 3662
        ::::::::|||   ::::::::::::         :::::::::
1176 rIleSerGlyAsnThrValSerValSerAlaThrGlyAspLeuThrThrL 1193

3663 CTACCGCCAACAAACCGACCTGCGCCAAATCGGTATGCAGAAAAACCTCG 3712
       :::::::::|||      :::   ::::::   ::::::   ||||||
1193 ysSerGlySerLysIleGluAlaLysSerGlyGluAlaAsnValThrSer 1209

3713 GCAGCGGGCGCGTCGGCATCCTGTTTTCGCACAACCGGACCGAAAACANC 3762
     |||:::|||:::   ::::::         |||   :::   :::|||
1210 AlaThrGlyThrIleGlyGly.........ThrIleSerGlyAsnThrVa 1223

3763 TTCGACGACGGCATCGGCA.............................. 3781
      ::::::||||||:::|||
1223 lAsnValThrAlaAsnAlaGlyAspLeuThrValGlyAsnGlyAlaGluI 1240

3782 .....ACTCGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAAT..... 3820
          :::   :::|||      |||         :::||||||
1240 leAsnAlaThrGluGlyAlaAlaThrLeuThrAlaThrGlyAsnThrLeu 1256

3821 ACGGCATCGGCAGGTTCGACATCGGCATCAGCACGGGCGCGGGTTTTAGC 3870
     |||::::::||||||||||:::   :::|||:::::::::::::|||
1257 ThrThrGluAlaGlySerSerIleThrSerThrLysGlyGlnValAspLe 1273

3871 AGCGGCANTCTNTCAGACGGCATCGGAGGCAAAATCCGCCGCCGCGTGCT 3920
        |||      |||::::::|||   |||   |||      |||:::
1273 uLeuAla......GlnAsnGlySerIleAlaGlySerIleAsnAlaAlaA 1288

3921 GCATTACGGCATTCAGGCACGATACCGCGCCGGTTTCGGCGGATTCGGCA 3970
       :::|||               |||      :::   |||   |||
1288 snValThrLeuAsnThrThrGlyThrLeuThrThrValAlaGlySerAsp 1304

3971 TCGAACCGTACATCGGCGCAACGCGCTATTTCGTCCAAA 4009
        :::   |||||||:::      :::|||:::::::|||
1305 IleLysAlaThrSerGlyThrLeuValIleAsnAlaLys 1317
```

seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01848

seq_documentation_block:

```
ID   AAB01848 standard; Protein; 1477 AA.
XX
AC   AAB01848;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain 12 HMW2A protein, SEQ ID NO:71.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain 12.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52197.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Example 16; Fig 29A-N; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
XX
SQ   Sequence   1477 AA;
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alignment_scores:

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            Quality:  251.00              Length:   1450
              Ratio:  0.382                 Gaps:     67
 Percent Similarity:  45.310   Percent Identity: 19.172
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alignment_block:

US-09-303-518D-651 x AAB01848 ..

Align seg 1/1 to: AAB01848 from: 1 to: 1477

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    :::|||         |||   :::   |||:::::::::::::   ||||| .
158 LysAspAlaIleIleAsnThrAsnGlyPheThrAlaSerThrLeuAspIl 174

213 TGAGGTNTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAA. 261
    |:::      |||   |||::::::          ::::::||||||
174 eSerAsnGluAsnIleLysAlaArgAsnPheThrPheGluGlnThrLysA 191

262 ..........GCCCCGATGATTGATTTTTCTGTG......GTGTCGCGT 294
              |||   :::::::::   ::::::      |||::::::
191 spLysAlaLeuAlaGluIleValAsnHisGlyLeuIleThrValGlyLys 207
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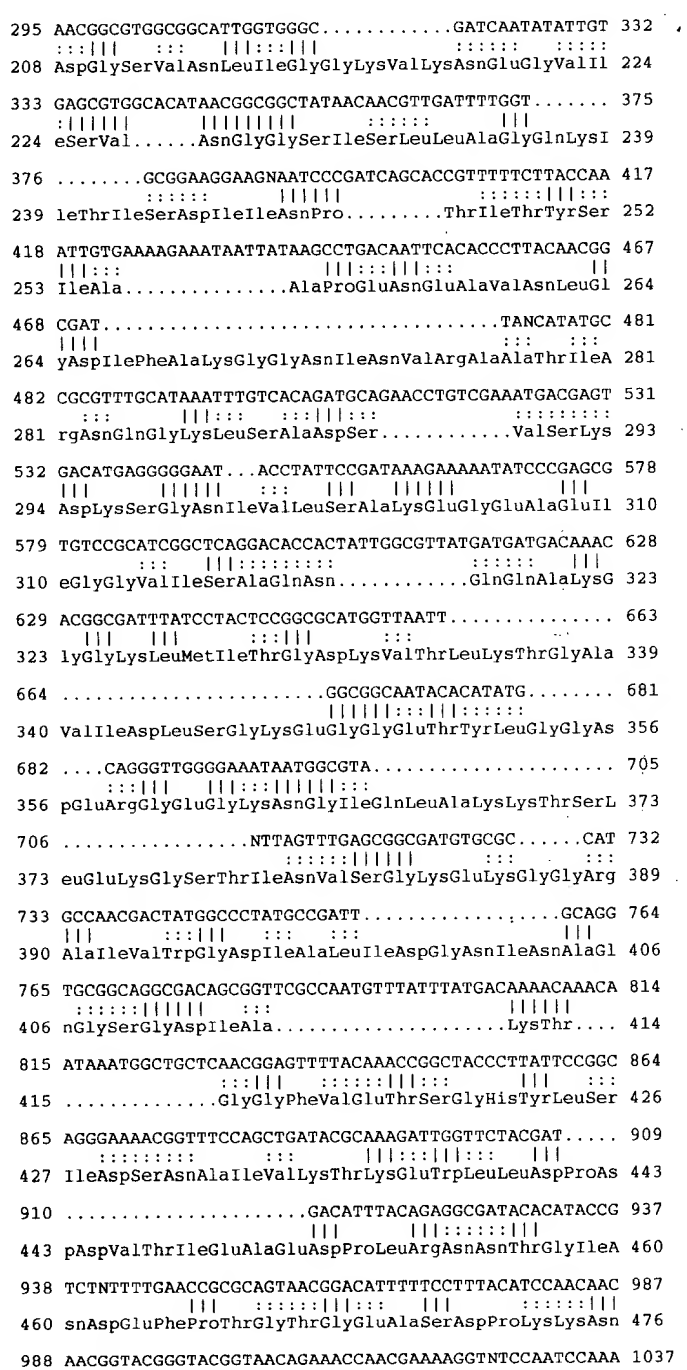
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208 AspGlySerValAsnLeuIleGlyGlyLysValLysAsnGluGlyValIl 224
333 GAGCGTGGCACATAACGGCGGCTATAACAACGTTGATTTTGGT..... 375
224 eSerVal.....AsnGlyGlySerIleSerLeuLeuAlaGlyGlnLysI 239
376 ........GCGGAAGGAAGNAATCCCGATCAGCACCGTTTTTCTTACCAA 417
239 leThrIleSerAspIleIleAsnPro.....ThrIleThrTyrSer 252
418 ATTGTGAAAAGAAATAATTATAAGCCTGACAATTCACACCCTTACAACGG 467
253 IleAla.....AlaProGluAsnGluAlaValAsnLeuGl 264
468 CGAT.....TANCATATGC 481
264 yAspIlePheAlaLysGlyGlyAsnIleAsnValArgAlaAlaThrIleA 281
482 CGCGTTTGCATAAATTTGTCACAGATGCAGAACCTGTCGAAATGACGAGT 531
281 rgAsnGlnGlyLysLeuSerAlaAspSer.....ValSerLys 293
532 GACATGAGGGGGAAT...ACCTATTCCGATAAAGAAAAATATCCCGAGCG 578
294 AspLysSerGlyAsnIleValLeuSerAlaLysGluGlyGluAlaGluIl 310
579 TGTCCGCATCGGCTCAGGACACCACTATTGGCGTTATGATGATGACAAAC 628
310 eGlyGlyValIleSerAlaGlnAsn.....GlnGlnAlaLysG 323
629 ACGGCGATTTATCCTACTCCGGCGCATGGTTAATT..... 663
323 lyGlyLysLeuMetIleThrGlyAspLysValThrLeuLysThrGlyAla 339
664 .....GGCGGCAATACACATATG..... 681
340 ValIleAspLeuSerGlyLysGluGlyGlyGluThrTyrLeuGlyGlyAs 356
682 ....CAGGGTTGGGGAAATAATGGCGTA..... 705
356 pGluArgGlyGluGlyLysAsnGlyIleGlnLeuAlaLysLysThrSerL 373
706 .....NTTAGTTTGAGCGGCGATGTGCGC.....CAT 732
373 euGluLysGlySerThrIleAsnValSerGlyLysGluLysGlyGlyArg 389
733 GCCAACGACTATGGCCCTATGCCGATT.....GCAGG 764
390 AlaIleValTrpGlyAspIleAlaLeuIleAspGlyAsnIleAsnAlaGl 406
765 TGCGGCAGGCGACAGCGGTTCGCCAATGTTTATTTATGACAAAACAAACA 814
406 nGlySerGlyAspIleAla.....LysThr.... 414
815 ATAAATGGCTGCTCAACGGAGTTTTACAAACCGGCTACCCTTATTCCGGC 864
415 .....GlyGlyPheValGluThrSerGlyHisTyrLeuSer 426
865 AGGGAAAACGGTTTCCAGCTGATACGCAAAGATTGGTTCTACGAT..... 909
427 IleAspSerAsnAlaIleValLysThrLysGluTrpLeuLeuAspProAs 443
910 .....GACATTTACAGAGGCGATACACATACCG 937
443 pAspValThrIleGluAlaGluAspProLeuArgAsnAsnThrGlyIleA 460
938 TCTNTTTTGAACCGCGCAGTAACGGACATTTTTCCTTTACATCCAACAAC 987
460 snAspGluPheProThrGlyThrGlyGluAlaSerAspProLysLysAsn 476
988 AACGGTACGGGTACGGTAACAGAAACCAACGAAAAGGTNTCCAATCCAAA 1037
477 SerGluLeuLysThr...ThrLeuThrAsnThrThrIleSerAsnTyrLe 492
1038 GCTTAAAGTACAGACAGTCCGACTGTTTGACGAATCTTTGAATGAAACTG 1087
492 uLysAsnAlaTrpThrMet.....AsnIleThrAlaSerA 504
1088 ATAAAGAACCAGTTTACGCGGCAGGGGGTGTTAATCAGTACCGTCCAAGG 1137
504 rgLysLeuThrValAsnSerSer..... 511
1138 TTAAACAACGGTGAAAACCTTTCTTTTATCGATTACGGCAACGGCAAACT 1187
512 IleAsnIleGlySerAsnSerHisLeuIleLeuHisSerLysGly..... 526
1188 CATCTTATCAAACAACATCAACCAAGGCGCGGGCGGTTTGTATTTTGAAG 1237
527 .....GlnArgGlyGlyGlyValGlnIleAspG 536
1238 GTGATTTTACGGTCTCGCCTGAAAACAACGAAACGTGGCAAGGCGCGGGC 1287
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553 ValAspValHisLysAsnIleThrLeu..... 561
1338 AAACGACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCA 1387
561 561
1388 AAGGGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTG 1437
562 .....AspGlnGlyPheLeuAsnIleThrAlaAlaSerValAlaPhe 575
1438 GATCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGG 1487
576 ...GluGlyGlyAsnAsnLysAlaArgAspAlaAlaAsnAlaLysIle.. 590
1488 CTTGNTCAGCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCA 1537
591 .....ValAlaGlnGlyThrValThrIleThrGlyGluGlyLys.... 603
1538 ACCCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAAC 1587
604 .....AspPheArgAlaAsnAsnValSerLeuAsn 613
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614 GlyThrGlyLysGlyLeuAsnIleIleSerSerValAsnAsn..... 627
1638 GATTGNCNATCATAATGCCACAACAACATCCACCGTTACCATTACAGGGA 1687
628 ....LeuThrHisAsn.....LeuSerGlyThrIleAsnIleSerGlyA 641
1688 ATGAAAGTATTACACAACCGAGTGGTAAG..... 1716
641 snIleThrIleAsnGlnThrThrArgLysAsnThrSerTyrTrpGlnThr 657
1717 .....AATATCAATAGACTTAATTACAGCAAAGAAAT 1748
658 SerHisAspSerHisTrpAsnValSerAlaLeuAsnLeu.....GluTh 672
1749 TGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGC 1798
672 rGlyAlaAsnPheThrPheIleLysTyrIleSerSerAsnSerLysGly. 688
1799 GGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCNGCTGCTT 1848
689 ..LeuThrThrGlnTyrArgSerSerAla..... 697
1849 TCCGGCGGAACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACT 1898

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3557 CCGTACAGGACGAATTGGACCGCGTGTTTGCCGAAGACCGCCGCAACGCN 3606
1157 IleAsnAlaThrAsnGlyLysAlaSerIleThrThrLysThrGlyAspIl 1173

3607 GTTTGGACAAGCNGCATCCGGNACACCAAACACTACCGTTCGC...AAGA 3653
1173 eSerGlyThrIleSerGlyAsnThrValSerValSerAlaThrGlyAspL 1190

3654 TTTCCGCGCCTACCGCCAACAAACCGACCTGCGCCAAATCGGTATGCAGA 3703
1190 euThrThrLysSerGlySerLysIleGluAlaLysSerGlyGluAlaAsn 1206

3704 AAAACCTCGGCAGCGGGCGCGTCGGCATCCTGTTTTCGCACAACCGGACC 3753
1207 ValThrSerAlaThrGlyThrIleGlyGly.....ThrIleSerGl 1220

3754 GAAAACANCTTCGACGACGGCATCGGCA.....;.... 3781
1220 yAsnThrValAsnValThrAlaAsnAlaGlyAspLeuThrValGlyAsnG 1237

3782 .....ACTCGGCACGGCTTGCCCACGGCGCCGTTTTCGGGC 3817
1237 lyAlaGluIleAsnAlaThrGluGlyAlaAlaThrLeuThrAlaThrGly 1253

3818 AAT......ACGGCATCGGCAGGTTCGACATCGGCATCAGCACGGGCGCG 3861
1254 AsnThrLeuThrThrGluAlaGlySerSerIleThrSerThrLysGlyGl 1270

3862 GGTTTTAGCAGCGGCANTCTNTCAGACGGCATCGGAGGCAAAATCCGCCG 3911
1270 nValAspLeuLeuAla......GlnAsnGlySerIleAlaGlySerIleA 1285

3912 CCGCGTGCTGCATTACGGCATTCAGGCACGATACCGCGCCGGTTTCGGCG 3961
1285 snAlaAlaAsnValThrLeuAsnThrThrGlyThrLeuThrThrValAla 1301

3962 GATTCGGCATCGAACCGTACATCGGCGCAACGCGCTATTTCGTCCAAA 4009
1302 GlySerAspIleLysAlaThrSerGlyThrLeuValIleAsnAlaLys 1317
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seq_documentation_block:

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XX
AC   AAW30291;
XX
DT   14-APR-1998  (first entry)
XX
DE   Non-typeable Haemophilus high mol.wt. surface protein HMW3.
XX
KW   Non-typeable Haemophilus; high molecular weight surface protein;
KW   HMW3; immunogen; vaccine; otitis media.
XX
OS   Haemophilus influenzae strain 5.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 113
FT                   /note= "encoded by GTG"
FT   Misc-difference 864
FT                   /note= "encoded by TGT"
XX
PN   WO9736914-A1.
XX
PD   09-OCT-1997.
XX
PF   01-APR-1997;   97WO-US04707.
XX
PR   01-APR-1996;   96US-0617697.
XX
PA   (BARE/) BARENKAMP S J.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1997-503038/46.
DR   N-PSDB; AAT90992.
XX
PT   High molecular weight proteins of non-typeable Haemophilus
PT   influenzae - useful for vaccine production
XX
PS   Claim 1; Page 93-97; 183pp; English.
XX
CC   This protein comprises the high molecular weight surface protein
CC   HMW3 (125 kDa) of non-typeable Haemophilus influenzae strain 5 that
CC   has the immunological ability to protect against disease caused by
CC   a non-typeable Haemophilus strain and is characterised by at least
CC   one surface-exposed B-cell epitope that is recognised by monoclonal
CC   antibody AD6.  The HMW3 amino acid sequence was deduced from an
CC   isolated hmw3 gene (see AAT90992).  HMW1 (see AAW30293), HMW2 (see
CC   AAW30294) and HMW4 (see AAW30292) have also been identified.  A
CC   conjugate comprising HMW3 linked to an antigen, hapten or
CC   polysaccharide, and a synthetic peptide of 6-150 amino acids
CC   corresponding to at least protective epitope of HMW3 are also
CC   claimed.  HMW proteins, conjugates and peptides can be used in
CC   vaccines, as immunogens for preparation of antibodies and as
CC   antigens for detection of these antibodies.
XX
SQ   Sequence   1598 AA;
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alignment_scores:

Quality:	251.00	Length:	1460
Ratio:	0.369	Gaps:	69
Percent Similarity:	46.644	Percent Identity:	20.616

alignment_block:
US-09-303-518D-651 x AAW30291 ..

Align seg 1/1 to: AAW30291 from: 1 to: 1598

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213 TGAGGTNTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAA. 261
174 eSerAsnGluAsnIleLysAlaArgAsnPheThrLeuGluGlnThrLysA 191

262 ..........GCCCCGATGATTGATTTTTCTGTG......GTGTCGCGT 294
191 spLysAlaLeuAlaGluIleValAsnHisGlyLeuIleThrValGlyLys 207

295 AACGGCGTGGCGGCATTGGTGGGC...........GATCAATATATTGT 332
208 AspGlySerValAsnLeuIleGlyGlyLysValLysAsnGluGlyValIl 224

333 GAGCGTGGCACATAACGGCGGCTATAACAACGTTGATTTTGGT..... 375
224 eSerVal......AsnGlyGlySerIleSerLeuLeuAlaGlyGlnLysI 239

376 ........GCGGAAGGAAGNAATCCCGATCAGCACCGTTTTTCTTACCAA 417
239 leThrIleSerAspIleIleAsnPro.........ThrIleThrTyrSer 252

418 ATTGTGAAAAGAAATAATTATAAGCCTGACAATTCACACCCTTACAACGG 467
253 IleAla..............AlaProGluAsnGluAlaIleAsnLeuGl 264

468 CGAT.................................TANCATATGC 481
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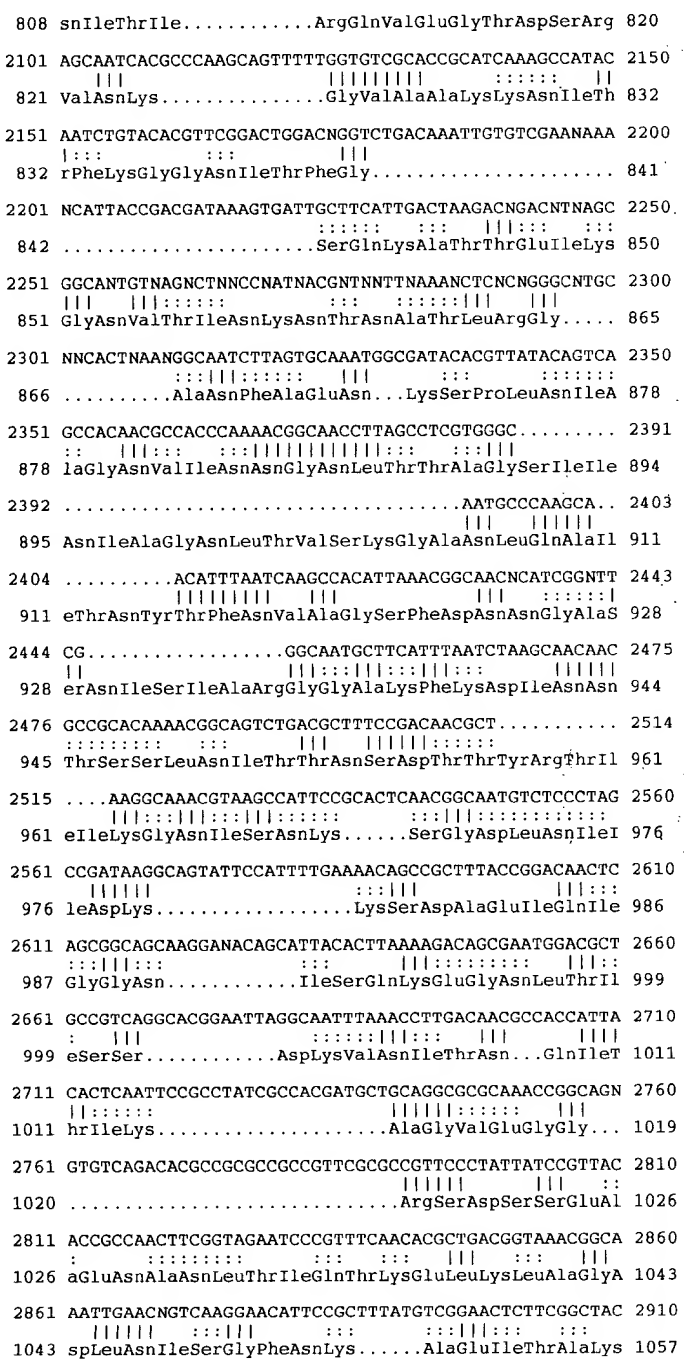
808 snIleThrIle.....ArgGlnValGluGlyThrAspSerArg 820
2101 AGCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCATAC 2150
821 ValAsnLys.....GlyValAlaAlaLysLysAsnIleTh 832
2151 AATCTGTACACGTTCGGACTGGACNGGTCTGACAAATTGTGTCGAANAAA 2200
832 rPheLysGlyGlyAsnIleThrPheGly..... 841
2201 NCATTACCGACGATAAAGTGATTGCTTCATTGACTAAGACNGACNTNAGC 2250
842 .....SerGlnLysAlaThrThrGluIleLys 850
2251 GGCANTGTNAGNCTNNCCNATNACGNTNNTTNAAANCTCNCNGGGCNTGC 2300
851 GlyAsnValThrIleAsnLysAsnThrAsnAlaThrLeuArgGly..... 865
2301 NNCACTNAANGGCAATCTTAGTGCAAATGGCGATACACGTTATACAGTCA 2350
866 .....AlaAsnPheAlaGluAsn...LysSerProLeuAsnIleA 878
2351 GCCACAACGCCACCCAAAACGGCAACCTTAGCCTCGTGGGC..... 2391
878 laGlyAsnValIleAsnAsnGlyAsnLeuThrThrAlaGlySerIleIle 894
2392 .....AATGCCCAAGCA.. 2403
895 AsnIleAlaGlyAsnLeuThrValSerLysGlyAlaAsnLeuGlnAlaIl 911
2404 .....ACATTTAATCAAGCCACATTAAACGGCAACNCATCGGNTT 2443
911 eThrAsnTyrThrPheAsnValAlaGlySerPheAspAsnAsnGlyAlaS 928
2444 CG.....GGCAATGCTTCATTTAATCTAAGCAACAAC 2475
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2476 GCCGCACAAAACGGCAGTCTGACGCTTTCCGACAACGCT..... 2514
945 ThrSerSerLeuAsnIleThrThrAsnSerAspThrThrTyrArgThrIl 961
2515 ....AAGGCAAACGTAAGCCATTCCGCACTCAACGGCAATGTCTCCCTAG 2560
961 eIleLysGlyAsnIleSerAsnLys.....SerGlyAspLeuAsnIleI 976
2561 CCGATAAGGCAGTATTCCATTTTGAAAACAGCCGCTTTACCGGACAACTC 2610
976 leAspLys.....LysSerAspAlaGluIleGlnIle 986
2611 AGCGGCAGCAAGGANACAGCATTACACTTAAAAGACAGCGAATGGACGCT 2660
987 GlyGlyAsn.....IleSerGlnLysGluGlyAsnLeuThrIl 999
2661 GCCGTCAGGCACGGAATTAGGCAATTTAAACCTTGACAACGCCACCATTA 2710
999 eSerSer.....AspLysValAsnIleThrAsn...GlnIleT 1011
2711 CACTCAATTCCGCCTATCGCCACGATGCTGCAGGCGCGCAAACCGGCAGN 2760
1011 hrIleLys.....AlaGlyValGluGlyGly... 1019
2761 GTGTCAGACACGCCGCGCCGCCGTTCGCGCCGTTCCCTATTATCCGTTAC 2810
1020 .....ArgSerAspSerSerGluAl 1026
2811 ACCGCCAACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCA 2860
1026 aGluAsnAlaAsnLeuThrIleGlnThrLysGluLeuLysLeuAlaGlyA 1043
2861 AATTGAACNGTCAAGGAACATTCCGCTTTATGTCGGAACTCTTCGGCTAC 2910
1043 spLeuAsnIleSerGlyPheAsnLys.....AlaGluIleThrAlaLys 1057
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1058 AsnGlySerAspLeuThrIleGlyAsnAlaSerGlyGly..... 1070
2961 GGCGGTCAACAATACCGGCAACGAACCCGTAAGCCTCGATCAATTGACGG 3010
1071 .....AsnAlaAspAlaLysLysValThrPheAspLysVal.... 1082
3011 TAGTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCACC 3060
1083 .....LysAspSerLysIleSerThrAspGlyHisAsnValThr 1095
3061 CTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACTCATCCG 3110
1096 LeuAsnSerGlu..... 1099
3111 CAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTT 3160
1100 .....ValLysThrSerAsnGlyS 1106
3161 CCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAAC 3210
1106 erSerAsnAlaGly.....AsnAspAsn 1113
3211 GCGCAAAGCCTTGACGCGCTGATTGCGGCCGGGCGCGATGCCGCCGAAAA 3260
1114 SerThrGlyLeu..... 1117
3261 GACAGAAAGCGTTGCCGAACCGGCCCGGCNGGCAGGCGGGGAAAATGTCG 3310
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1158 y.SerValGluValThrAlaGlnAsnGlyThrIleLysGlyAsnIleThr 1174
3461 AACCGCAACCTCAACCCCAACCGCAGCGCGACCTGATNAGCCGTTATGCC 3510
1175 SerGlnAsnValThrVal.....ThrAlaThrGluAsnLeuValThrTh 1189
3511 AATAGCGGTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTTTTCGCCGT 3560
1189 rGluAsnAlaValIleAsnAlaThrSerGlyThrValAsnIleSer.... 1204
3561 ACAGGACGAATTGGACCGCGTGTTTGCCGAAGACCGCCGCAACGCNGTTT 3610
1205 .....ThrLysThrGlyAspIleLysGly 1212
3611 GGA...CAAGCNGCATCCGGNACACCAAACACTACCGTTCGC..... 3649
1213 GlyIleGluSerThrSerGlyAsnValAsnIleThrAlaSerGlyAsnTh 1229
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3696 TATGCAGAAAAACCTCGGCAGCGGGCGCGTCGGCATCCTGTTTTCGCACA 3745
1246 laGlyAlaLeuThrThrThrAlaGlySerThrIleSerAla.....Thr 1260
3746 ACCGGA..... 3751
1261 ThrGlyAsnAlaAsnIleThrThrLysThrGlyAspIleAsnGlyLysVa 1277

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     3752 ....CCGAAAACANCTTCGACGACGGCATCGGCAACTCGGCACGGCTTGC 3797
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     3798 CCACGGCGCCGTTTTCGGGCAAT.............ACGGCATCGGCAGGT 3835
            ::::::   :::||||||||||            ||||||:::::|||
     1294 laValGlyAsnIleSerGlyAsnThrValThrIleThrAlaAspSerGly 1310

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     1327 rThrSerSerGlnSerGlyAspIleGluGlyThrIleSerGlyAsnThrV 1344

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     1344 alAsnValThrAlaSerThrGlyAspLeuThrIleGlyAsnSerAlaLys 1360

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     1361 ValGluAlaLysAsnGlyAlaAlaThrLeuThrAlaGluSerGlyLysLe 1377

     4015 GATTACCGCTACGAAAACGTCAATATCG 4042
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seq_documentation_block:

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AC   AAW30294;
XX
DT   14-APR-1998  (first entry)
XX
DE   Non-typeable Haemophilus high mol.wt. surface protein HMW2.
XX
KW   Non-typeable Haemophilus; high molecular weight surface protein;
KW   HMW2; hmw2A gene; immunogen; vaccine; otitis media.
XX
OS   Haemophilus influenzae strain 12.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 34
FT                   /note= "encoded by TTC"
FT   Misc-difference 35
FT                   /note= "encoded by CGC"
FT   Misc-difference 36
FT                   /note= "encoded by TAT"
FT   Misc-difference 37
FT                   /note= "encoded by GTT"
FT   Misc-difference 38
FT                   /note= "encoded by ACT"
FT   Misc-difference 39
FT                   /note= "encoded by ATC"
FT   Misc-difference 40
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PD   09-OCT-1997.
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PF   01-APR-1997;   97WO-US04707.
XX
PR   01-APR-1996;   96US-0617697.
XX
PA   (BARE/) BARENKAMP S J.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1997-503038/46.
DR   N-PSDB; AAT90995.
XX
PT   High molecular weight proteins of non-typeable Haemophilus
PT   influenzae - useful for vaccine production
XX
PS   Claim 7; Page 73-78; 183pp; English.
XX
CC   This protein comprises the high molecular weight surface protein
CC   HMW2 (123 kDa) of non-typeable Haemophilus influenzae strain 12 that
CC   has the immunological ability to protect against disease caused by a
CC   non-typeable Haemophilus strain and is characterised by at least
CC   one surface-exposed B-cell epitope that is recognised by monoclonal
CC   antibody AD6.  The HMW2 amino acid sequence was deduced from the
CC   hmw2 gene sequence (see AAT90995 and AAT90997).  The expressed protein
CC   is truncated, starting at residue 442 of the full-length gene
CC   product.  HMW1 (see AAW30293), HMW3 (see AAW30291) and HMW4 (see
CC   AAW30292) have also been identified.  A conjugate comprising HMW2
CC   linked to an antigen, hapten or polysaccharide, and a synthetic
CC   peptide of 6-150 amino acids corresponding to at least protective
CC   epitope of HMW2 are also claimed.  HMW proteins, conjugates and
CC   peptides can be used in vaccines, as immunogens for preparation of
CC   antibodies and as antigens for detection of these antibodies.
XX
SQ   Sequence   1477 AA;
```

alignment_scores:

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            Quality:  250.50              Length:   1399
              Ratio:  0.403                 Gaps:     66
 Percent Similarity:  44.389   Percent Identity: 19.085
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alignment_block:

US-09-303-518D-651 x AAW30294 ..

Align seg 1/1 to: AAW30294 from: 1 to: 1477

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     178 AATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTNTACAACAA 227
         |||:::||||||:::::::::          |||            :::||
     282 AsnGlnGlyLysLeuSerAla.........AspSerValSerLysAspLy 295

     228 AAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGATT 277
         |:::|||::::::|||   ::::::                  |||
     295 sSerGlyAsnIleValLeuSerAlaLysGluGlyGluAlaGluIleGlyG 312

     278 TTTCTGTGGTGTCGCGTAAC..............GGCGTGGCGGCATTG 312
```

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312 lyValIleSerAlaGlnAsnGlnGlnAlaLysGlyGlyLysLeuMetIle 328

313 GTGGGCGATCAATATATTGTGAGCGTG.....................GC 341
329 ThrGlyAspLysValThrLeuLysThrGlyAlaValIleAspLeuSerGl 345

342 ACATAACGGCGGC......TATAACAACGTTGATTTTGGTGCGGAAGGAA 385
345 yLysGluGlyGlyGluThrTyrLeuGlyGlyAspGluArgGlyGluGlyL 362

386 GNAATCCCGATCAGCACCGTTTTTCTTACCAAATTGTGAAAAGAAATAAT 435
362 ysAsn..................GlyIleGlnLeuAlaLysLys..... 370

436 TATAAGCCTGACAATTCACACCCTTACAACGGCGATTANCATATGCCGCG 485

370 ..................................................... 370

486 TTTGCATAAATTTGTCACAGATGCAGAACCTGTCGAAATGACGAGTGACA 535
371 .....................................ThrSerLeuG 374

536 TGAGGGGGAATACC......TATTCCGATAAAGAAAAATATCCCGAGCGT 579
374 luLysGlySerThrIleAsnValSerGlyLysGluLys..... 386

580 GTCCGCATCGGCTCAGGACACCACTATTGGCGTTATGATGATGACAAACA 629
387 .........GlyGlyArgAlaIleValTrp..................... 393

630 CGGCGATTTATCCTACTCCGGCGCATGGTTAATTGGCGGCAATACACATA 679
394 .GlyAspIleAla..............LeuIleAspGlyAsnIleAsnA 405

680 TGCAGGGTTGGGGAAATAATGGCGTANTTAGTTTGAGCGGCGATGTGCGC 729
405 laGlnGly.........................SerGlyAspIleAla 412

730 CATGCCAACGACTATGGCCCTATGCCGATTGCAGGTGCGGCAGGCGACAG 779
413 LysThr.....................GlyGlyPheValGluThrSe 421

780 CGGTTCGCCAATGTTTATTTATGACAAAACAAACAATAAATGGCTGCTCA 829
421 rGlyHisAspLeuPheIleLysAsp.....................A 430

830 ACGGAGTTTTACAAACCGGCTACCCTTATTCCGGCAGGGAAAACGGTTTC 879
430 snAlaIleValAspAla................................ 435

880 CAGCTGATACGCAAAGATTGGTTCTACGATGACATTTACAGAGGCGATAC 929
436 ............LysGluTrpLeuLeuAsp..................... 441

930 ACATACCGTCTNTTTTGAACCGCGCAGTAACGGACATTTTTCCTTTACAT 979
442 ............PheAspAsnValSerIleAsnAlaGluAspProLeuP 454

980 CCAACAACAACGGT.................ACGGGTACGGTAACAGAA 1011
454 heAsnAsnThrGlyIleAsnAspGluPheProThrGlyThr...GlyGlu 469

1012 ACCAACGAAAAGGTNTCCAATCCAAAGCTTAAAGTACAGACAGTCCGACT 1061
470 AlaSerAspProLysLysAsnSerGluLeuLysThrThrLeuThr..... 484

1062 GTTTGACGAATCTTTGAATGAAACTGATAAAGAACCAGTTTACGCGGCAG 1111
485 ..............AsnThrThrIleSerAsnTyrLeuLysAsnAlaT 496

1112 GGGGTGTTAATCAGTACCGTCCAAGG.........TTAAACAACGGTGAA 1152
496 rpThrMetAsnIleThrAlaSerArgLysLeuThrValAsnSerSerIle 512

1153 AACCTTTCTTTTATCGATTACGGCAACGGCAAACTCATCTTATCAAACAA 1202
513 AsnIleGly............SerAsnSerHisLeuIleLeuHisSerLy 525

1203 CATCAACCAAGGCGCGGGCGGTTTGTATTTTGAAGGTGATTTTACGGTCT 1252
525 s...GlyGlnArgGlyGlyGlyValGlnIleAspGlyAspIleThrSerL 541

1253 CGCCTGAAAACAACGAAACGTGGCAAGGCGCGGGCGTTCATATCAGTGAA 1302
541 ysGlyGlyAsnLeuThrIleTyrSerGlyGlyTrpValAspValHisLys 557

1303 GACAGTACCGTTACTTGGAAAGTAAACGGCGTGGCAAACGACCGCCTGTC 1352
558 AsnIleThrLeu..................................... 561

1353 CAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGGGAAAACCAAG 1402
562 .....................................AspGlnG 564

1403 GCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCAGGCAGAC 1452
564 lyPheLeuAsnIleThrAlaAlaSerValAlaPhe...GluGlyGlyAsn 579

1453 GATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGNTCAGCGGCAG 1502
580 AsnLysAlaArgAspAlaAlaAsnAlaLysIle.........ValAlaGl 593

1503 GGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAACTCT 1552
593 nGlyThrValThrIleThrGlyGluGlyLys................... 603

1553 ATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCTTTCG 1602
604 .....AspPheArgAlaAsnAsnValSerLeuAsnGlyThrGlyLysGly 618

1603 TTCCACCGTATTCAAAATACCGATGAAGGGGCGATGATTGNCNATCATAA 1652
619 LeuAsnIleIleSerSerValAsnAsn............LeuThrHisAs 631

1653 TGCCACAACAACATCCACCGTTACCATTACAGGGAATGAAAGTATTACAC 1702
631 n......LeuSerGlyThrIleAsnIleSerGlyAsnIleThrIleAsnG 646

1703 AACCGAGTGGTAAG..................................... 1716
646 lnThrThrArgLysAsnThrSerTyrTrpGlnThrSerHisAspSerHis 662

1717 ...AATATCAATAGACTTAATTACAGCAAAGAAATTGCCTACAACGGTTG 1763
663 TrpAsnValSerAlaLeuAsnLeu......GluThrGlyAlaAsnPheTh 677

1764 GTTTGGCGAGAAAGATACGACCAAAACGAACGGGCGGCTCAACCTTGTTT 1813
677 rPheIleLysTyrIleSerSerAsnSerLysGly...LeuThrThrGlnT 693

1814 ACCAGCCCGCCGCAGAAGACCGCACCCNGCTGCTTTCCGGCGGAACAAAT 1863
693 yrArgSerSerAla.........................GlyValAsn 700

1864 TTAAACGGCAACATCACGCAAACAAACGGCAAACTGTTTTTC........ 1905
701 PheAsnGly............ValAsnGlyAsnMetSerPheAsnLeuLy 713

1906 .....................................................A 1906
713 sGluGlyAlaLysValAsnPheLysLeuLysProAsnGluAsnMetAsnT 730

1907 GCGGCAGACCGACACCGCACGCCTAC....................... 1932
730 hrSerLysProLeuProIleArgPheLeuAlaAsnIleThrAlaThrGly 746
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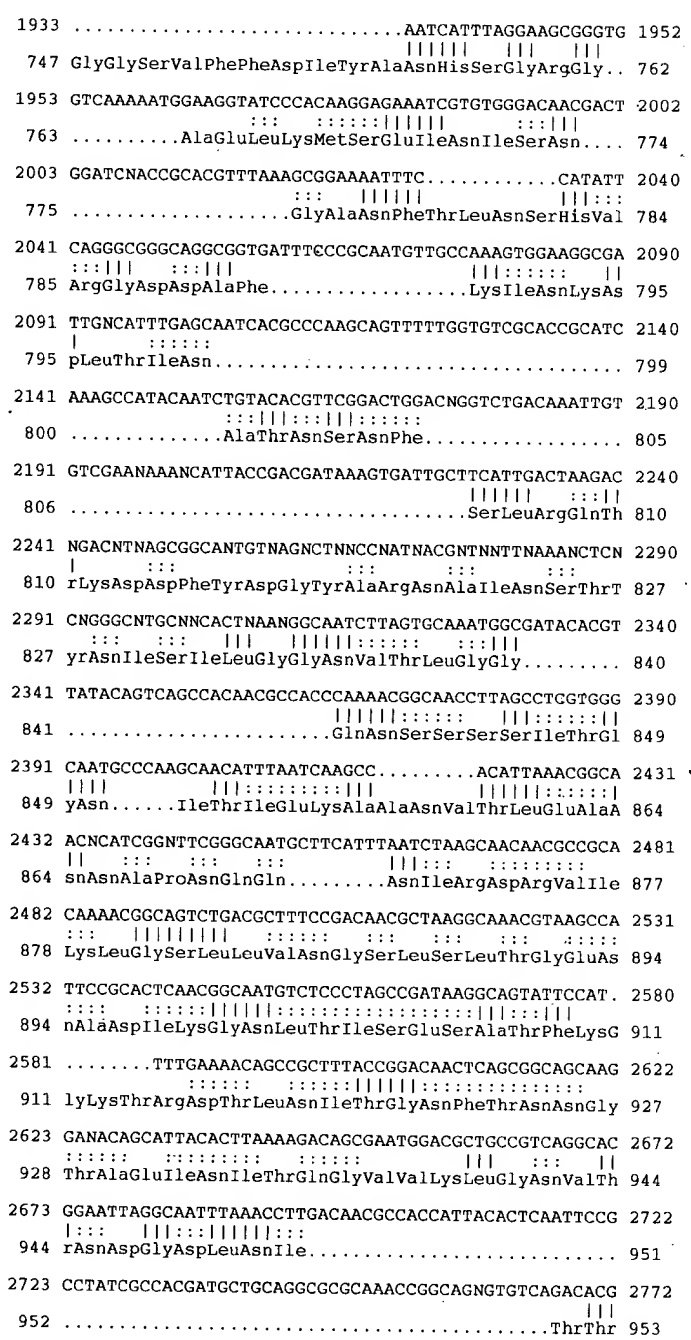

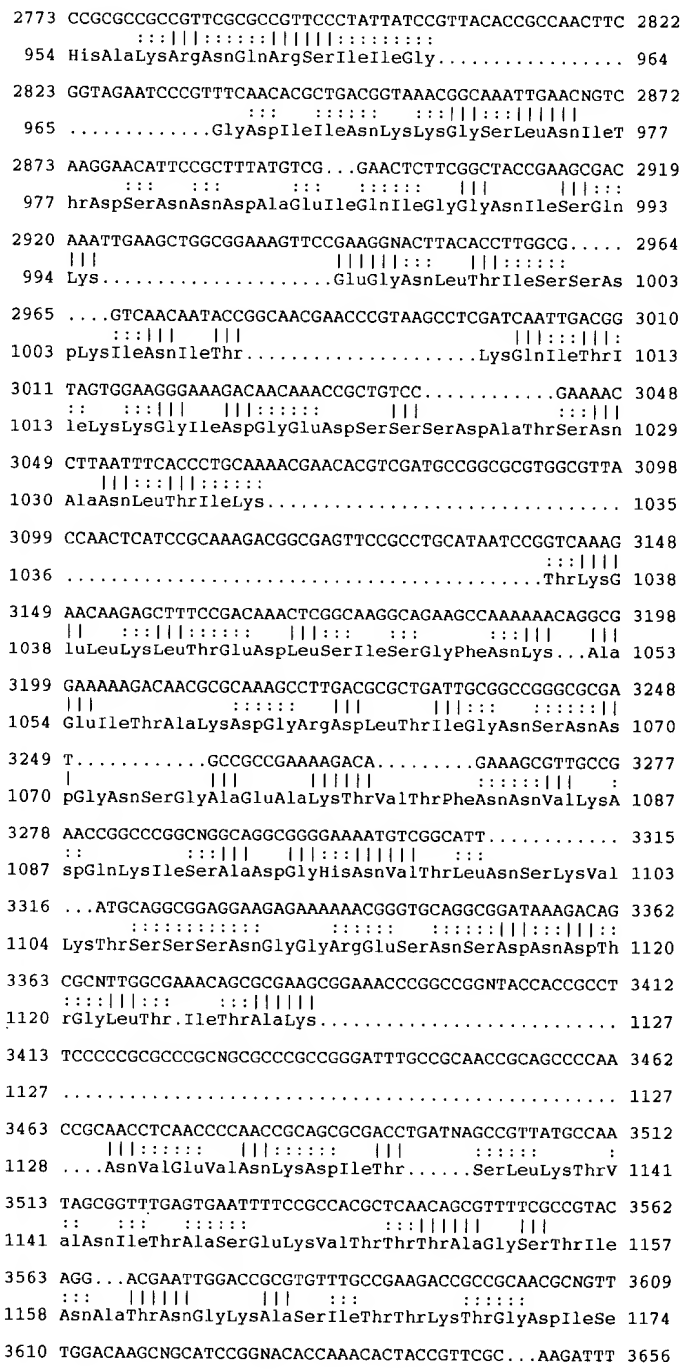

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 3657 CCGCGCCTACCGCCAACAAACCGACCTGCGCCAAATCGGTATGCAGAAAA 3706
      :::::   :::::::::|||      :::   ::::::   ::::::
 1191 hrThrLysSerGlySerLysIleGluAlaLysSerGlyGluAlaAsnVal 1207

 3707 ACCTCGGCAGCGGGCGCGTCGGCATCCTGTTTTCGCACAACCGGACCGAA 3756
      ||||||||||:::|||:::   ::::::          |||   :::   ::
 1208 ThrSerAlaThrGlyThrIleGlyGly.........ThrIleSerGlyAs 1221

 3757 AACANCTTCGACGACGGCATCGGCA..................... 3781
      :|||   ::::::||||||:::|||
 1221 nThrValAsnValThrAlaAsnAlaGlyAspLeuThrValGlyAsnGlyA 1238

 3782 ...........ACTCGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAAT 3820
                 :::   :::|||      |||         :::|||||
 1238 laGluIleAsnAlaThrGluGlyAlaAlaThrLeuThrAlaThrGlyAsn 1254

 3821 ......ACGGCATCGGCAGGTTCGACATCGGCATCAGCACGGGCGCGGGT 3864
            |||::::::||||||||||:::   :::|||:::::::::::||
 1255 ThrLeuThrThrGluAlaGlySerSerIleThrSerThrLysGlyGlnVa 1271

 3865 TTTAGCAGCGGCANTCTNTCAGACGGCATCGGAGGCAAAATCCGCCGCCG 3914
      |        |||      |||::::::|||   |||   |||      |
 1271 lAspLeuLeuAla......GlnAsnGlySerIleAlaGlySerIleAsnA 1286

 3915 CGTGCTGCATTACGGCATTCAGGCACGATACCGCGCCGGTTTCGGCGGAT 3964
      ||:::   :::|||               |||      :::   |||
 1286 laAlaAsnValThrLeuAsnThrThrGlyThrLeuThrThrValAlaGly 1302

 3965 TCGGCATCGAACCGTACATCGGCGCAACGCGCTATTTCGTCCAAA 4009
      |||      :::   ||||||:::      :::|||:::::::|||
 1303 SerAspIleLysAlaThrSerGlyThrLeuValIleAsnAlaLys 1317

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seq_documentation_block:
ID   ABG30355 standard; Protein; 1606 AA.
XX
AC   ABG30355;
XX
DT   18-FEB-2002  (first entry)
XX
DE   Novel human diagnostic protein #30346.
XX
KW   Human; chromosome mapping; gene mapping; gene therapy; forensic;
KW   food supplement; medical imaging; diagnostic; genetic disorder.
XX
OS   Homo sapiens.
XX
PN   WO200175067-A2.
XX
PD   11-OCT-2001.
XX
PF   30-MAR-2001; 2001WO-US08631.
XX
PR   31-MAR-2000; 2000US-0540217.
PR   23-AUG-2000; 2000US-0649167.
XX
PA   (HYSE-) HYSEQ INC.
XX
PI   Drmanac RT,  Liu C,  Tang YT;
XX
DR   WPI; 2001-639362/73.
DR   N-PSDB; AAS94542.
XX
PT   New isolated polynucleotide and encoded polypeptides, useful in
PT   diagnostics, forensics, gene mapping, identification of mutations
PT   responsible for genetic disorders or other traits and to assess
PT   biodiversity  -
XX
PS   Claim 20; SEQ ID No 60714; 103pp; English.
XX
CC   The invention relates to isolated polynucleotide (I) and
CC   polypeptide (II) sequences. (I) is useful as hybridisation probes,
CC   polymerase chain reaction (PCR) primers, oligomers, and for chromosome
CC   and gene mapping, and in recombinant production of (II). The
CC   polynucleotides are also used in diagnostics as expressed sequence tags
CC   for identifying expressed genes. (I) is useful in gene therapy techniques
CC   to restore normal activity of (II) or to treat disease states involving
CC   (II). (II) is useful for generating antibodies against it, detecting or
CC   quantitating a polypeptide in tissue, as molecular weight markers and as
CC   a food supplement. (II) and its binding partners are useful in medical
CC   imaging of sites expressing (II). (I) and (II) are useful for treating
CC   disorders involving aberrant protein expression or biological activity.
CC   The polypeptide and polynucleotide sequences have applications in
CC   diagnostics, forensics, gene mapping, identification of mutations
CC   responsible for genetic disorders or other traits to assess biodiversity
CC   and to produce other types of data and products dependent on DNA and
CC   amino acid sequences. ABG00010-ABG30377 represent novel human
CC   diagnostic amino acid sequences of the invention.
CC   Note: The sequence data for this patent did not appear in the printed
CC   specification, but was obtained in electronic format directly from WIPO
CC   at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ   Sequence   1606 AA;

alignment_scores:
           Quality:  242.50              Length:    739
             Ratio:  0.691                Gaps:     31
 Percent Similarity:  47.497   Percent Identity: 19.892

alignment_block:
 US-09-303-518D-651 x ABG30355   ..

 Align seg 1/1  to: ABG30355  from: 1  to: 1606

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  632 GlyThrLeuThrValAsnAspAsnGlyLysAlaThr..............  643

 2361 CACCCAAAACGGCAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATTTA 2410
                          ::::::|||   |||:::   |||:::::::
  644 ...................AspIleValGlnAsnSerGlyAlaAlaLeuG  654

 2411 ATCAAGCCACATTAAACGGCAACNCATCGGNTTCGGGCAAT......... 2451
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  654 lnThrSerThrAlaAsnGly...IleGluIleSerGlyThrHisGlnTyr  669

 2452 GCTTCATTTAATCTAAGCAACAACGCCGCACAAAAC.............. 2487
      ::::::|||::::::|||:::|||   |||   |||
  670 GlyThrPheSerIleSerGlyAsnLeuAlaThrAsnMetLeuLeuGluAs  686

 2488 ....GGCAGTCTGACGCTTTCCGACAACGCTAAGGCAAACGTAAGCCATT 2533
          |||:::|||   :::      ::::::::::|||:::   |||
  686 nGlyGlyAsnLeuLeuValLeuAlaGlyThrGluAlaArgAspSerThrV  703

 2534 CCGCACTCAACGGCAATGTCTCCCTAGCCGATAAGGCAGTATTCCATTTT 2583
        :::   :::|||                        |||:::   ::::::
  703 alGlyLysGlyGly.....................AlaMetGlnAsnLeu  712

 2584 GAAAACAGCCGCTTTACCGGACAACTCAGCGGCAGCAAGGANACAGCATT 2633
        ::::::      |||         ||||||::::::   |||
  713 GlyGlnAspSerAlaThrLysValAsnSerGlyGlyGlnTyrThrLeuGl  729

 2634 ACACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAATTA.... 2679
       :::   ||||||:::      :::|||      :::   :::|||
  729 yArgSerLysAspGluPheGlnAlaLeuAlaArgAlaGluAspLeuGlnV  746

 2679 ..................................................  2679

  746 alAlaGlyGlyThrAlaIleValTyrAlaGlyThrLeuAlaAspAlaSer  762

 2680 ..............GGCAATTTAAACCTT................... 2694
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                    |||:::|||:::|||
 763 ValSerGlyAlaThrGlySerLeuSerLeuMetThrProArgAspAsnVa 779

2695 .....GACAACGCCACCA 2707
                    |||:::|||||||:
 779 lThrProValLysLeuGluGlyAlaValArgIleThrAspSerAlaThrL 796

2708 TTACACTCAATTCCGCCTAT.....CGCCACGATGCTGCAGGCGCG 2748
     ::|||||::::::::       |||   :::::|||
 796 euThrLeuGlyAsnGlyValAspThrThrLeuAlaAspLeuThrAlaAla 812

2749 CAAACCGGCAGNGTG.....TCAGACACGCC 2774
     :::   |||:::|||       :::   |||
 813 SerArgGlySerValTrpLeuAsnSerAsnAsnSerCysAlaGlyThrSe 829

2775 GCGCCGCCGTTCGCGC...CGTTCCCTATTA..... 2802
      :::   :::   |||   :::||||||||||
 829 rAsnCysGluTyrArgValAsnSerLeuLeuLeuAsnAspGlyAspValT 846

2803 ..........TCCGTTACACCGCCAACTTCGGTAGAATCCCGTTTCAAC 2841
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 846 yrLeuSerAlaGlnThrAlaAlaProAlaThrThrAsnGlyIleTyrAsn 862

2842 ACGCTGACGGTAAACGGCAAATTGAACNGTCAAGGAACATTCCGCTTTAT 2891
     |||||||||:::|||   :::|||:::   :::|||:::|||   :::
 863 ThrLeuThrThrAsn...GluLeuSerGlySerGlyAsnPheTyrLeuHi 878

2892 GTCGGAACTCTTCGGCTACCGAAGCGACAAATTGAAGCTGGCGGAAAGTT 2941
      :::::::::   |||   |||:::|||:::|||   :::   :::::::
 878 sThrAsnValAlaGlySerArgGlyAspGlnLeuValValAsnAsnAsnA 895

2942 CCGAAGGNACTTACACCTTGGCGGTCAACAATACCGGCAACGAACCCGTA 2991
     ::   |||::::::   :::   |||:::::||||||   :::|||
 895 laThrGlyAsnPheLysIlePheValGlnAspThrGlyValSerProGln 911

2992 AGCCTCGATCAATTGACGGTAGTGGAAGGGAAAGACAACAAACCGCTGTC 3041
     |||   |||   :::|||:::   ||||||
 912 SerAspAspAlaMetThrLeuGlyGluGly.....Me 922

3042 CGAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGATGCCGGCGCGT 3091
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 922 tLeuArgLeuArgTrpAlaIleProAlaValSerValAspLeuGlyThrT 939

3092 GGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCG 3141
     :::::|||   :::::::::::::||||||  :::|||
 939 yrGluTyr...ValLeuLysSerAspGly.ThrSer..... 949

3142 GTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAGAAGCCAAAAA 3191

 949 ..... 949

3192 ACAGGCGGAAAAAGACAACGCGCAAAGCCTTGACGCGCTGATTGCGGCCG 3241
                    :::   :::|||||||:::   ::::::|||
 950 ..................AsnTrpThrLeuThrAsnAspValLysPro 959

3242 GGCGCGATGCCGCCGAAAAGACAGAAAGCGTTGCCGAACCGGCCCGGCNG 3291
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 960 AsnProAspPro.................IleProAsn..... 966

3292 GCAGGCGGGGAAAATGTCGGCATTATGCAGGCGGAGGAAGAGAAAAAACG 3341

 966 ..... 966

3342 GGTGCAGGCGGATAAAGACAGCGCNTTGGCGAAACAGCGCGAAGCGGAAA 3391
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 967 .....ProLys 968

3392 CCCGGCCGGNTACCACCGCCTTCCCCCGCGCCCGCNGCGCCCGCCGGGAT 3441
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 969 ProAspProLysProAspProLysProAspPro..AsnProLys..... 982

3442 TTGCCGCAACCGCAGCCCCAACCGCAACCTCAACCCCAACCGCAGCGCGA 3491
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 983 ...ProAspProThrProAspProThrProThrProValProGluLysAr 998

3492 CCTGATNAGCCGTTATGCCAATAGCGGTTTGAGTGAATTTTCCGCCACGC 3541
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 998 gIleThrPro......SerThrAlaAlaValLeuAsnMetAlaAlaThrL 1013

3542 TCAACAGCGTTTTC.............GCCGTACAGGACGAATTGGAC 3576
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1013 euProLeuValPheAspAlaGluLeuAsnSerIleArgGluArgLeuAsn 1029

3577 CGCGTGTTTGCCGAAGACCGCCGCAACGCNGTTTGGACAAGCNGCATCCG 3626
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1030 IleMetLysAlaSerProAsnAsnAsnAsnValTrpGlyAlaThrTyrAs 1046

3627 GNACACCAAACACTACCGTTCGCAAGATTTCCGCGCCCTACCGCCAACAAA 3676
     ::::   ::::::       ::::::          :::|||:::|||
1046 nThrArgAsnAsnValThrThrAspAlaGlyAlaGlyTyrGluGlnThrL 1063

3677 CCGACCTGCGCCAAATCGGTATGCAGAAAAAC.....CTCGGC 3714
                  :::|||::::::::::::              |||
1063 euThrGlyMetThrValGlyIleAspSerArgAsnAspIleProGluGly 1079

3715 AGCGGGCGCGTCGGCATCCTGTTTTCGCACAACCGGACCGAAAACANCTT 3764
               :::|||   :::::::::::::::::::::::   :::||
1080 IleThrThrLeuGlyAlaPheMetGlyTyrSerHisSerHisIleSerPh 1096

3765 CGACGACGGCATCGGCAACTCGGCACGGCTTGCCCACGGCGCCGTTTTCG 3814
     ||||   |||                  :::||||||:::|||   |
1096 eAspArgGly.....GlyHisGlySerVal...G 1105

3815 GGCAATACGGCATCGGC..... 3831
     ||:::|||::::::|||
1105 lySerTyrSerLeuGlyGlyTyrAlaSerTrpGluHisGluSerGlyPhe 1121

3832 .....AGGTTCGACATCGGCATC..... 3849
                        ||||||      ::::::
1122 TyrLeuAspGlyValValLysLeuAsnArgPheLysSerAsnValAlaGl 1138

3850 .......AGCACGGGCGCGGGTTTTAGCAGCGGCANTCTNTCAGACGGCA 3892
           |||:::|||::::::   :::::::::      |||:::|||:
1138 yLysMetSerSerGlyGlyAlaAlaAsnGlySerTyrHisSerAsnGlyL 1155

3893 TCGGAGGCAAAATCCGCCGCCGCGTGCTGCATTACGGCATTCAGGCACGA 3942
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1155 euGlyGlyHis.....IleGluThrGly 1162

3943 TACCGCGCCGGTTTCGGCGGATTCGGCATCGAACCGTACATCGGCGCAAC 3992
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1163 MetArgPheThrAspGlyAsnTrpAsnLeuThrProTyrAlaSerLeuTh 1179

3993 GCGCTATTTCGTCCAAAAAGCGGATTACCGCTACGAAAAC..... 4032
     |   :::   :::::::::   :::|||:::   :::|||
1179 rGlyPheThrAlaAspAsnProGluTyrHisLeuSerAsnGlyMetLysS 1196

4033 ..GTCAATATCGCCACCCCCGGTCTTGCGTTCAACCGNTACCGN...GCG 4077
          ::::::   |||   ::::::            ||||||
1196 erLysSerValAspThrArgSerIle.....TyrArgGluLeu 1208

4078 GGCATTAAGGCAGATTATTCATTCAAACCGGCGCAACACATNTCCATCAC 4127
     |||          :::|||::::::::::   ::::::      ::::::
1209 GlyAlaThrLeuSerTyrAsnMetArgLeuGlyAsnGlyMetGluValGl 1225

4128 NCCTTATTTNAGCCTGTCCTATACCGATGCCGCTTCGGGCAAAGTCCGAA 4177
      |||:::   :::   :::                          |||:
1225 uProTrpLeuLysAlaAlaValArgLysGluPheValAspAspAsnArgV 1242

4178 CACGCGTCAATACC 4191
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1242 alLysValAsnSer 1246
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seq_documentation_block:

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ID   AAU34143 standard; Protein; 2086 AA.
XX
AC   AAU34143;
XX
DT   14-FEB-2002  (first entry)
XX
DE   Staphylococcus aureus cellular proliferation protein #419.
XX
KW   Antisense; prokaryotic cellular proliferation protein;
KW   antibiotic; antibacterial; drug design.
XX
OS   Staphylococcus aureus.
XX
PN   WO200170955-A2.
XX
PD   27-SEP-2001.
XX
PF   21-MAR-2001; 2001WO-US09180.
XX
PR   21-MAR-2000; 2000US-191078P.
PR   23-MAY-2000; 2000US-206848P.
PR   26-MAY-2000; 2000US-207727P.
PR   23-OCT-2000; 2000US-242578P.
PR   27-NOV-2000; 2000US-253625P.
PR   22-DEC-2000; 2000US-257931P.
PR   16-FEB-2001; 2001US-269308P.
XX
PA   (ELIT-) ELITRA PHARM INC.
XX
PI   Haselbeck R,  Ohlsen KL,  Zyskind JW,  Wall D,  Trawick JD,  Carr GJ;
PI   Yamamoto RT,  Xu HH;
XX
DR   WPI; 2001-611495/70.
DR   N-PSDB; AAS52002.
XX
PT   New polynucleotides for the identification and development of
PT   antibiotics, comprise sequences of antisense nucleic acids -
XX
PS   Example 3; Seq ID No 5639; 511pp; English.
XX
CC   The invention relates to antisense inhibitors of genes essential to
CC   prokaryotic cellular proliferation, their use in identifying the
CC   genes, their use in the discovery of novel antibiotics, the essential
CC   genes themselves and the encoded proteins. The prokaryotes used are
CC   Escherichia coli, Staphylococcus aureus, Salmonella typhi, Klebsiella
CC   pneumoniae, Pseudomonas aeruginosa and Enterococcus faecalis. The
CC   invention is also useful for the identification of potential new targets
CC   for antibiotic development. The antisense nucleic acids can also be used
CC   to identify proteins used in proliferation, to express these proteins,
CC   and to obtain antibodies capable of binding to the expressed proteins.
CC   The proteins can be used to screen compounds in rational drug discovery
CC   programmes. The antisense nucleic acid sequence is also useful to screen
CC   for homologous nucleic acids which are required for cell proliferation in
CC   a wide variety of organisms. The present sequence represents an
CC   essential prokaryotic cellular proliferation protein.
CC   Note: The sequence data for this patent did not form part
CC   of the printed specification, but was obtained in electronic
CC   format directly from WIPO at
CC   ftp.wipo.int/pub/published_pct_sequences.
XX
SQ   Sequence   2086 AA;


alignment_scores:
            Quality:  241.50              Length:   1531
              Ratio:  0.325                Gaps:     71
 Percent Similarity:  48.465   Percent Identity: 20.248

alignment_block:
 US-09-303-518D-651 x AAU34143   ..

 Align seg 1/1  to: AAU34143  from: 1  to: 2086
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231 AGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGATTTTT 280
    :::|||   |||:::   |||:::|||::::::   :::||| ||||||:
 28 GlnGlySerGlyGluThrIleSerAspGluGlnArgSerAsp.AspPheT 44

281 CTGTGGTGTCG..................................... 291
    ::|||||:::
 44 hrValValAlaProGlnProAsnHisAlaAsnThrLysIleTrpGlnAsn 60

292 .....CGTAACGGCGTGGCGGCATTGGTGGGCGA 320
                  :::|||      :::   |||:::::
 61 GlyHisIleAspIleThrProAsnAsnProSerGlyHisLeuIleAsnPr 77

321 TCAATATATTGTGAGCGTGGCACATAACGGCGGCTATAACAACGTTGATT 370
              :::::::::|||::::::         :::|||
 77 oThrGlnAlaMetAspIleAlaTyrThrGluLysMetGlyAsn....... 91

371 TTGGTGCGGAAGGAAGNAATCCCGATCAGCACCGTTTTTCTTACCAAATT 420
      |||||||||                |||      :::   ::::::
 92 ..GlyAlaGlu.................HisSerLysThrIleAsnVal 101

421 GTGAAAAGAAATAAT.................TATAAGCCTGACAATTC 452
    |||:::   :::|||                  |||||||||
102 ValArgGlyGlnAsnAsnGlnTrpThrIleAlaAsnLysProAsp..... 116

453 ACACCCTTACAACGGCGATTANCATATGCCGCGTTTGCATAAATTTGTCA 502
                                                 :::||||
117 .....................................TyrValT 119

503 CA...GATGCAGAACCTGTCGAAATGACGAGTGACATGAGGGGGAATACC 549
    ||   |||||||:::      :::::::|||      :::::::::||||||
119 hrLeuAspAlaHisThrGlyLysValThr......PheAsnAlaAsnThr 133

550 TATTCCGATAAAGAAAAATATCCCGAGCGTGTCCGCATCGGCTCAGGACA 599
      :::   ::::::                 :::   |||:::|||||
134 ValLysProAsnSerAlaIleThrIleThrProLysAlaGlyThrGlyHi 150

600 CCACTATTGGCGTTATGATGATGACAAACACGGCGATTTATCCTACTCCG 649
    |                                  :::   |||   :::
150 s.............................SerAlaSerSerAsnP 156

650 GCGCATGGTTAATTGGCGGCAATACACAT..................... 678
      :::   |||   :::      ||||||
156 roSerThrLeuThrAlaProAlaThrHisThrValAsnThrThrGluIle 172

679 ATGCAGGGTTGGGGAAATAAT...GGCGTANTTAGTTTGAGCGGCGATGT 725
    ::::::   :::|||:::|||      :::::::::::::::::   ||
173 ValLysAspTyrGlySerAsnValThrAlaAlaGluIleAsnAsnAlaVa 189

726 GCGCCATGCCAACGACTATGGCCCTATGCCGATTGCAGGTGCGGCAGGCG 775
    |:::   ||||||                              |||:::
189 lGlnValAlaAsnLys.................ArgThrAlaThrIleL 200

776 ACAGCGGTTCGCCAATGTTTATTTATGACAAAACAAACAATAAATGGCTG 825
      :::|||:::   |||                ||||||:::   |||
200 ysAsnGlyThrAlaMet.............ProThrAsn.LeuAlaGlyGl 212

826 CTCAACGGAGTTTTACAAACCGGCTACCCTTATTCCGGCAGGGAAAACGG 875
     ||||||                 |||   |||||||::      |||
212 ySerThr.................ThrThrIleProValThrValThrT 223

876 TTTCCAGCTGATACGCAAAGATTGGTTCTACGATGACATTTACAGAGGCG 925
      ::::::               |||||||||            |||:::
223 yrAsnAsp..............GlySerThrGluGluValGlnGluSer 234

926 ATACACATACCGTCTNTTTTGAACCGCGCAGTAACGGA.......CATTT 968
    |||         :::      ::::::   :::|||         |||::
235 IlePheThrLysAlaAspLysArgGluLeuIleThrAlaLysAsnHisLe 251

969 TTCCTTTACATCCAACAACAACGGT......ACGGGTACGGTAACAGAAA 1012
    ::::         :::::::::|||         ||||||:::|||:::
251 uAspAspProValSerThrAspGlyLysLysProGlyThrIleThrGlnT 268

1013 CCAACGAAAAGGTNTCCAATCCAAAGCTTAAAGTACAGACAGTCCGACTG 1062
```

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      |||:::   :::   |||   :::   :::::::::|||::::::
  268 yrAsnAsnAlaIleHisAsnAlaGlnGlnGlnIleAsnThrAlaLysThr 284

 1063 ...TTTGACGAATCTTTGAATGAAACTGATAAAGAACCAGTTTACGCGGC 1109
        ::::::   :::|||:::          |||      :::::
  285 GluAlaGlnGlnValIleAsnAsnGluArgAlaThrProGlnGlnValSe 301

 1110 AGGGGGTGTTAATCAGTACCGT.........CCAAGGTTAAACAACGGTG 1150
      :   ::::::::::::   |||       ::::::|||:::::::
  301 rAspAlaLeuThrLysValArgAlaAlaGlnThrLysIleAsnGluAlaL 318

 1151 AAAACCTTTCTTTTATCGATTACGGCAACGGCAAACTCATCTTATCAAAC 1200
      ::   |||                 |||::::::|||:::   |||:::
  318 ysAlaLeuLeuGlnAsnLysGluAspAsnSerGlnLeuValThrSerLys 334

 1201 AAC..............ATCAACCAA..................... 1212
      |||              :::||||||
  335 AsnAsnLeuGlnSerSerValAsnGlnValProSerThrThrGlyMetTh 351

 1213 ....................GGCGCGGGCGGTTTGTATTTTGAAGGTG 1240
                          :::|||          |||   :
  351 rGlnGlnSerIleAspAsnTyrAsnAlaLysLysArgGluAlaGluThrG 368

 1241 ATTTTACGGTCTCGCCTGAAAACAACGAAACGTGGCAAGGCGCGGGCGTT 1290
      :::::|||::::::   :::      ::::::   ::::::::::::
  368 luIleThrAlaAlaGlnArgValIleAspAsnGlyAspAlaThrAlaGln 384

 1291 CATATCAGTGAAGACAGTACCGTTACTTGGAAAGTAAACGGCGTGGCAAA 1340
      :::||||||:::::::::|||::::::   :::              ||
  385 GlnIleSerAspGluAsnThrThrAlaGlnArg.............As 396

 1341 CGACCGCCTGTCCAAAATCGGCAAAGGCACG......CTGCACGTTCAA. 1383
      ||||      :::::::|||:::::::::|||           |||:::
  396 nAspLeuThrAsnGlnIleSerGlnAlaThrAsnLeuAlaAlaValGluS 413

 1384 ............................GCCAAAGGGGAAAACCAA 1401
                                 |||   |||:::   |||
  413 erValLysGlnSerAlaAsnSerLeuAspGlyAlaMetGlyAsnLeuGln 429

 1402 GGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCAGGCAGA 1451
         :::|||:::      :::|||||||:::      ::::::      ||
  430 ThrAlaIleAsnAspLysSerGlyThrLeuAlaSerGlnAsnPheLeuAs 446

 1452 C...GATAAAGGCAAAAAACAAGCCTTTAGTGAA.............. 1482
      |   |||:::   |||::::::|||:::::::::
  446 pAlaAspGluGlnLysArgAsnAlaTyrAsnGlnAlaValSerAsnAlaG 463

 1483 ........ATCGGCTTGNTCAGCGGCAGGGGTACGGTGCAACTGAATGCC 1524
              ::::::      :::|||   :::|||::::::      :::
  463 luThrIleLeuAsnLysGlnThrGlyProAsnThrAlaLysThrAlaVal 479

 1525 GATAATCAGTTCAACCCCGACAAACTCTATTTCGGCTTTCGCGGCGGACG 1574
      ::::::   :::|||
  480 GluGlnAlaLeuAsn................................ 484

 1575 TTTGGATTTAAACGGGCATTCGCTTTCGTTCCACCGTATTCAAAATACCG 1624
           ::::::|||:::   :::   :::::::::      ||||||
  485 ....AsnValAsnSerAlaLysHisAlaLeuAsnGlyThrGlnAsn.... 498

 1625 ATGAAGGGGCGATGATTGNCNATCATAATGCCACAACAACATCCACCGTT 1674
                           :::|||||||      ::::::   :::
  499 ....................LeuAsnAsnAlaLysGlnAlaAlaIleThr 508

 1675 ACCATTACAGGGAATGAAAGTATTACACAACCGAGTGGTAAGAATATCAA 1724
      :::|||:::|||   ::::::::::::|||   :::         :::::
  509 AlaIleAsnGlyAlaSerAspLeuAsnGlnLysGlnLysAspAlaLeuLy 525

 1725 TAGACTTAATTACAGCAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGA 1774
      :           :::   :::   :::   |||:::         ::::
  525 sAlaGlnAlaAsnGlyAlaGlnArgValSerAsnAlaGlnAspValGlnA 542

 1775 AAGATACGACCAAAACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCC 1824
      ::::::::|||:::   |||      ::::::   :::   :::   |||
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  542 rgAsnAlaThrGluLeuAsnThrAlaMetGlyThrLeu...LysHisAla 557

 1825 GCAGAAGACCGCACCCNGCTGCTTTCCGGCGGAACAAATTTAAACGGCAA 1874
           |||:::|||      |||:::::::::      :::||||:::::
  558 IleAlaAspLysThrAsnThrLeuAlaSerSerLysTyrValAsnAlaAs 574

 1875 CATCACGCAA.......................ACAAACGGCAAACTGT 1900
      :   |||:::                       ||||||::::::   :
  574 pSerThrLysGlnAsnAlaTyrThrThrLysValThrAsnAlaGluHisI 591

 1901 TTTTCAGCGGCAGACCGACA.......................CCGCAC 1926
      :::::||||||   ||||||
  591 leIleSerGlyThrProThrValValThrThrProSerGluValThrAla 607

 1927 GCCTACAATCATTTAGGAAGCGGGTGGTCAAAAATGGAAGGTATCCCACA 1976
      |||   |||::::::::::|||:::   ::::::::::::|||      ::
  608 AlaAlaAsnGlnValAsnSerAlaLysGlnGluLeuAsnGlyAspGluAr 624

 1977 AGGAGAAATCGTGTGGGACAAC..............GACTGGATCNACC 2011
      :   :::::::::   :::|||                |||   :::::::
  624 gLeuArgValAlaLysGlnAsnAlaAsnThrAlaIleAspAlaLeuThrG 641

 2012 GC......ACGTTTAAAGCGGAAAATTTCCATATTCAGGGCGGGCAGGCG 2055
      ::      |||   :::      ::::::      |||   |||||||||
  641 lnLeuAsnThrProGlnLysAlaLysLeuLysGluGlnValGlyGlnAla 657

 2056 GTGATTTCCCGCAATGTTGCCAAAGTGGAAGGCGATTGNCATTTGAGCAA 2105
               :::::::::      |||:::   :::   :::      ||
  658 AsnArgLeuGluAspIleGlnThrValGlnThrAsnGlyGlnAlaLeuAs 674

 2106 TCACGCC.......................................... 2112
      |:::|||
  674 nAsnAlaMetLysGlyLeuArgAspSerIleAlaAsnGluThrThrValL 691

 2113 ........CAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCATACAATC 2154
              |||            ::::::|||:::::::::   |||
  691 ysAlaSerGlnAsnTyrThrAspAlaSerProAsnAsnGlnSerThrTyr 707

 2155 TGTACACGT...TCGGACTGGACNGGTCTGACAAATTGTGTCGAANAAAN 2201
         :::      |||:::      |||:::   |||   ::::::
  708 AsnSerAlaValSerAsnAlaLysGlyIleIleAsnGlnThrAsnAsnPr 724

 2202 CATTACCGACGATAAAGTGATTGCTTCATTGACT.............. 2235
              |||   :::::::|||::::::   |||
  724 oThrMetAspThrSerAlaIleThrGlnAlaThrThrGlnValAsnAsnA 741

 2236 ..AAGACNGACNTNAGCGGCANTGTNAGNCTNNCCNATNACGNTNNTTNA 2283
        |||:::      :::|||:::      |||      :::      :::
  741 laLysAsnGlyLeuAsnGlyAlaGluAsnLeuArgAsnAlaGlnAsnThr 757

 2284 AAN.........CTCNCNGGGCNTGCNNCACTNAANGGCAAT........ 2316
      :::          |||          :::   |||::::::|||
  758 AlaLysGlnAsnLeuAsnThrLeuSerHisLeuThrAsnAsnGlnLysSe 774

 2317 ....CTTAGTGCAAATGGCGAT..............ACACGTTATACAG 2347
          :::|||::::::   |||               ::::::   |||:
  774 rAlaIleSerSerGlnIleAspArgAlaGlyHisValSerGluValThrA 791

 2348 TCAGCCACAACGCC..............ACCCAAAACGGCAACCTTAGC 2382
      :::::   ||||||              ||||||   |||||||||:::
  791 laAlaLysAsnAlaAlaThrGluLeuAsnThrGlnMetGlyAsnLeuGlu 807

 2383 CTCGTGGGCAATGCCCAAGCAACATTTAATCAAGCCACATTAAACGGCAA 2432
         :::   :::   |||   |||   :::|||::::::         ||
  808 GlnAlaIleHisAspGlnAsnThrValLysGlnGlyVal.........As 821

 2433 CNCATCGGNTTCGGGCAATGCTTCATTTAATCTAAGCAACAACGCCGCAC 2482
      |   :::   :::   :::|||:::   :::      :::||||||::::
  821 nPheThrAspAlaAspLysAlaLysArgAspAlaTyrThrAsnAlaValS 838

 2483 AAAACGGCAGTCTGACGCTTTCCGACAACGCTAAGGCAAACGTAAGC... 2529
      ::::::::::      |||:::   :::      ||||||:::|||
  838 erArgAlaGluThrIleLeuAsnLysThrGlnGlyAlaAsnThrSerLys 854
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2530 .....CATTCCGCACT 2540
                 :::|||||
 855 GlnAspValGluAlaAlaIleGlnAsnValThrSerAlaLysAsnAlaLe 871

2541 CAACGGC......AATGTCTCCCTAGCCGATAAGGCAGTATTCCATTTTG 2584
     |||||||      ||||||:::   |||   :::::::::   |||
 871 uAsnGlyAspGlnAsnValThrAsnAlaLysAsnThrAlaLysHisAlaL 888

2585 AAAACAGCCGCTTTACCGGACAACTCAGCGGCAGCAAGGANACAGCATTA 2634
       |||:::           :::::::::::::::::          |||
 888 euAsnAsn......LeuThrSerIleAsnAsnAlaGlnLysArgAspLeu 902

2635 CACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAA..... 2676
          |||   ::::::   |||      :::|||:::|||
 903 ThrThrLysIleAspGlnAlaThrThrValAlaGlyValGluAlaValSe 919

2677 .....TTAGGCAATTTA......AACC 2692
                          ::::::||||||      ::::
 919 rAsnThrGlyThrGlnLeuAsnThrAlaMetAlaAsnLeuGlnAsnGlyI 936

2693 TTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCTGCA 2742
     ::::::::   :::   ||||||   |||         |||||||||
 936 leAsnAspLysAlaAsnThrLeuAlaSerGluAsnTyrHisAspAlaAsp 952

2743 GGC............GCGCAAACCGGCAGNGTGTCAGACACGCCGCGCCG 2780
     :::            |||   |||   :::|||:::::::::   :::
 953 SerAspLysLysThrAlaTyrThrGlnAlaValThrAsnAlaGluAsnIl 969

2781 CCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAAT 2830
          ::::::::::|||      |||              ::::::||||||:
 969 eLeuAsnLysAsnSer...GlySerAsnLeuAspLysAlaAlaValGluA 985

2831 CCCGTTTCAACACGCTGACG.............GTAAACGGC..... 2859
     ::   ::::::   :::|||              :::|||||
 985 snAlaLeuSerGlnValThrAsnAlaLysGlyAlaLeuAsnGlyAsnHis 1001

2860 ..............AAATTGAACNGTCAAGGAACATTCCGCTTTATGTC 2894
                    |||   |||:::::::   |||:::::::   :::::
1002 AsnLeuGluGlnAlaLysSerAsnAlaAsnThrThrIleAsnGlyLeuGl 1018

2895 GGAACTCTTCGGCTACCGAAGCGACAAATTGAAG.............. 2928
     ::::|||          ::::::||||||||||||
1018 nHisLeuThrThrAlaGlnLysAspLysLeuLysGlnGlnValGlnGlnA 1035

2929 .....CTGGCGGAAAGTTCCGAAGGNACTTAC 2955
                          ::::::||||||   :::|||
1035 laGlnAsnValAlaGlyValAspThrValLysSerSerAlaAsnThrLeu 1051

2956 ACCTTGGCGGTCAACAATACCGGCAACGAACCCGTAAGCCTCGATCAATT 3005
     :::   |||:::::::::      |||         |||:::::::::
1052 AsnGlyAlaMetGlyThrLeuArgAsn.....SerIleGlnAspAs 1065

3006 GACGGTAGTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAATT 3055
      |||:::::::::::   :::|||          :::   :::   |||
1065 nThrAlaThrAsnAsnGlyGlnAsnTyrLeuAspAlaThrGluSerAsnL 1082

3056 TCACCCTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACTC 3105
       |||      |||:::   ||||||::: |||:::||||||   |||::
1082 ysThrAsnTyrAsnAsnAlaValAspSer.AlaAsnGlyValIleAsnAl 1098

3106 ATCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCGG.............. 3142
     ::::::::::         :::|||      |||:::
1098 aThrSerAsnProAsnMetAspAlaAsnAlaIleAsnGlnIleAlaThrG 1115

3143 ..........TCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAG 3181
               :::||||||            |||:::::      |||
1115 lnValThrSerThrLysAsnAlaLeuAspGlyThrHisAsnLeuThrGln 1131

3182 AAGCCAAAAAACAGGCGGAAAAA......GACAACGCGCAAAGCCTT... 3222
       ||||||:::   |||   :::      |||:::|||   :::|||
1132 ..AlaLysGlnThrAlaThrAsnAlaIleAspGlyAlaThrAsnLeuAsn 1147
```

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3223 ............GACGCGCTGATTGCGGCCGGGCGCGATGCCGCCGAAAA 3260
                 |||||||||      |||         :::|||:::::
1148 LysAlaGlnLysAspAlaLeu...LysAlaGlnValThrSerAlaGlnAr 1163

3261 GACAGAAAGCGTTGCCGAACCGGCCCGGCNGGCAGGCGGGGAAAATGTCG 3310
     ::::   :::|||::::::      ::::::|||:::      |||::::
1163 gValAlaAsnValThrSerIleGlnGlnThrAlaAsnGluLeuAsnThrA 1180

3311 GCATTATGCAGGCGGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGAC 3360
     :::::   |||   ::::::                ::|||   |||:::
1180 laMetGlyGlnLeuGlnHisGlyIleAspAspGluAsnAlaThrLysGln 1196

3361 AGCGCNTTGGCGAAACAGCGCGAAGCGGAAACCCGGCCGGNTACCACCGC 3410
     :::         |||   |||:::||||||   :::         |||||
1197 Thr......GlnLysTyrArgAspAlaGlu...GlnSerLysLysThrAl 1210

3411 CTTCCCCCGCGCCCGCNGCGCCCGCCGGGATTTGCCGCAACCGCAGCCCC 3460
     |:::   :::|||   :::|||   :::   :::   :::   |||
1210 aTyrAspGlnAlaValAlaAlaAlaLysAlaIleLeuAsnLysGlnThrG 1227

3461 AACCGCAACCTCAACCCCAACCGCAGCGCGACCTGATNAGCCGTTATGCC 3510
                                                  :::
1227 ly.....Ser 1228

3511 AATAGCGGTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTTTTCGCCGT 3560
     ||||||      :::      :::   :::|||:::::::|||   :::::
1229 AsnSerAspLysAlaAlaValAspArgAlaLeuGlnGlnValThrSerTh 1245

3561 ACAGGACGAATTGGACCGCGTGTTTGCCGAAGACCGCCGCAACGCNGTTT 3610
     ::::|||   |||:::                |||   :::   |||
1245 rLysAspAlaLeuAsn.....GlyAspAlaLysLeuAlaGlu. 1257

3611 GGACAAGCNGCATCCGGNACACCAAACACTACCGTTCGCAAGATTTCCGC 3660
     ::::::||||||:::                          |||   :::
1258 AlaLysAlaAlaAla.....LysGlnAsnLe 1266

3661 GCCTACCGCCAACAAACCGACCTGCGCCAAATCGGTATGCAGAAAAACCT 3710
        |||   |||       |||   |||             ::::::|||:
1266 uGlyThrLeuAsnHisIleThrAsnAla.....GlnArgThrA 1279

3711 CGGCAGCGGGCGCGTCGGCATCCTGTTTTCGCACAACCGGACCGAAAACA 3760
     ::       |||          ::::::      :::   |||   :::|||
1279 laLeuGluGlyGlnIleAsnGlnAlaThrThrValAspGlyValAsnThr 1295

3761 NCTTCGACGACGGCATCGGCAACTCGGCACGGCTTGCCCACGGCGCCGTT 3810
        :::|||:::|||::::::          ::::::   :::
1296 ValLysThrAsnAlaAsnThrLeuAspGlyAlaMetAsnSerLeuGlnGl 1312

3811 TTCGGGCAATACGGCATCGGCAGGTTCGACATCGGCATCAGCACGGGCGC 3860
      |||   |||       :::|||
1312 ySerIleAsnAspLysAspAla..... 1319

3861 GGGTTTTAGCAGCGGCANTCTNTCAGACGGCATCGGAGGCAAAA...TCC 3907
       :::|||                  |||:::|||:::|||   :::
1320 ..ThrLeuArgAsnGlnAsnTyrLeuAspAlaAspGluSerLysArgAsn 1335

3908 GCCGCCGCGTGCTGCATTACGGCATTCAGG..... 3937
     |||   :::   ::::::|||||||   :::
1336 AlaTyrThrGlnAlaValThrAlaAlaGluGlyIleLeuAsnLysGlnTh 1352

3938 ....CACGATACCGCGCCGGTTTCGGCGGATTCGGCATCGAACCGT...A 3980
           :::|||:::   :::::::::|||:::|||   |||       |
1352 rGlyGlyAsnThrSerLysAlaAspValAspAsnAlaLeuAsnThrValT 1369

3981 CATCGGCGCAACGCGCTATTTCGTCCAAAAAGCGGATTACCGCTACGAAA 4030
     ||   |||:::   |||::::::::::   :::::::::      ||||||
1369 hrArgAlaLysAlaAlaLeuAsnGlyAlaGluAsnLeuArgAsnThrLys 1385

4031 ACGTCAATATCGCCACCCCCGGTCTTGCGTTCAACCGNTACCGNGCGGGC 4080
     ||||||                    :::|||   |||   :::::
1386 ThrSer.....AlaThrAsnThrIleAsnGl 1394

4081 ATTAAGGCAGATTATTCATTCAAACCGGCGCAAC 4114
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      :|||   ::::::   :::   ::::::   |||
  1394 yLeuProAsnLeuThrGlnLeuGlnLysAspAsn 1405

seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:AAU37017

seq_documentation_block:
ID   AAU37017 standard; Protein; 5795 AA.
XX
AC   AAU37017;
XX
DT   14-FEB-2002  (first entry)
XX
DE   Staphylococcus aureus cellular proliferation protein #1187.
XX
KW   Antisense; prokaryotic cellular proliferation protein;
KW   antibiotic; antibacterial; drug design.
XX
OS   Staphylococcus aureus.
XX
PN   WO200170955-A2.
XX
PD   27-SEP-2001.
XX
PF   21-MAR-2001; 2001WO-US09180.
XX
PR   21-MAR-2000; 2000US-191078P.
PR   23-MAY-2000; 2000US-206848P.
PR   26-MAY-2000; 2000US-207727P.
PR   23-OCT-2000; 2000US-242578P.
PR   27-NOV-2000; 2000US-253625P.
PR   22-DEC-2000; 2000US-257931P.
PR   16-FEB-2001; 2001US-269308P.
XX
PA   (ELIT-) ELITRA PHARM INC.
XX
PI   Haselbeck R,  Ohlsen KL,  Zyskind JW,  Wall D,  Trawick JD,  Carr GJ;
PI   Yamamoto RT,  Xu HH;
XX
DR   WPI; 2001-611495/70.
DR   N-PSDB; AAS54876.
XX
PT   New polynucleotides for the identification and development of
PT   antibiotics, comprise sequences of antisense nucleic acids -
XX
PS   Example 3; Seq ID No 12610; 511pp; English.
XX
CC   The invention relates to antisense inhibitors of genes essential to
CC   prokaryotic cellular proliferation, their use in identifying the
CC   genes, their use in the discovery of novel antibiotics, the essential
CC   genes themselves and the encoded proteins. The prokaryotes used are
CC   Escherichia coli, Staphylococcus aureus, Salmonella typhi, Klebsiella
CC   pneumoniae, Pseudomonas aeruginosa and Enterococcus faecalis. The
CC   invention is also useful for the identification of potential new targets
CC   for antibiotic development. The antisense nucleic acids can also be used
CC   to identify proteins used in proliferation, to express these proteins,
CC   and to obtain antibodies capable of binding to the expressed proteins.
CC   The proteins can be used to screen compounds in rational drug discovery
CC   programmes. The antisense nucleic acid sequence is also useful to screen
CC   for homologous nucleic acids which are required for cell proliferation in
CC   a wide variety of organisms. The present sequence represents an
CC   essential prokaryotic cellular proliferation protein.
CC   Note: The sequence data for this patent did not form part
CC   of the printed specification, but was obtained in electronic
CC   format directly from WIPO at
CC   ftp.wipo.int/pub/published_pct_sequences.
XX
SQ   Sequence   5795 AA;


alignment_scores:
           Quality:  241.50            Length:   1531
             Ratio:  0.325               Gaps:     71
 Percent Similarity:  48.465   Percent Identity: 20.248

alignment_block:
 US-09-303-518D-651 x AAU37017   ..

 Align seg 1/1  to: AAU37017  from: 1  to: 5795

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    2305 GlnGlySerGlyGluThrIleSerAspGluGlnArgSerAsp.AspPheT 2321

     281 CTGTGGTGTCG..................................... 291
         ::||||||:::
    2321 hrValValAlaProGlnProAsnHisAlaAsnThrLysIleTrpGlnAsn 2337

     292 .....................CGTAACGGCGTGGCGGCATTGGTGGGCGA 320
                              :::|||      :::   |||::::::
    2338 GlyHisIleAspIleThrProAsnAsnProSerGlyHisLeuIleAsnPr 2354

     321 TCAATATATTGTGAGCGTGGCACATAACGGCGGCTATAACAACGTTGATT 370
                 ::::::::::|||:::::         :::|||
    2354 oThrGlnAlaMetAspIleAlaTyrThrGluLysMetGlyAsn....... 2368

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    2369 ..GlyAlaGlu.................HisSerLysThrIleAsnVal 2378

     421 GTGAAAAGAAATAAT.................TATAAGCCTGACAATTC 452
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     453 ACACCCTTACAACGGCGATTANCATATGCCGCGTTTGCATAAATTTGTCA 502
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     503 CA...GATGCAGAACCTGTCGAAATGACGAGTGACATGAGGGGGAATACC 549
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    2396 hrLeuAspAlaHisThrGlyLysValThr......PheAsnAlaAsnThr 2410

     550 TATTCCGATAAAGAAAAATATCCCGAGCGTGTCCGCATCGGCTCAGGACA 599
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    2427 s.............................SerAlaSerSerAsnP 2433

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    2450 ValLysAspTyrGlySerAsnValThrAlaAlaGluIleAsnAsnAlaVa 2466

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         |:::   ||||||                              |||:::
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    2477 ysAsnGlyThrAlaMet.............ProThrAsn.LeuAlaGlyGl 2489

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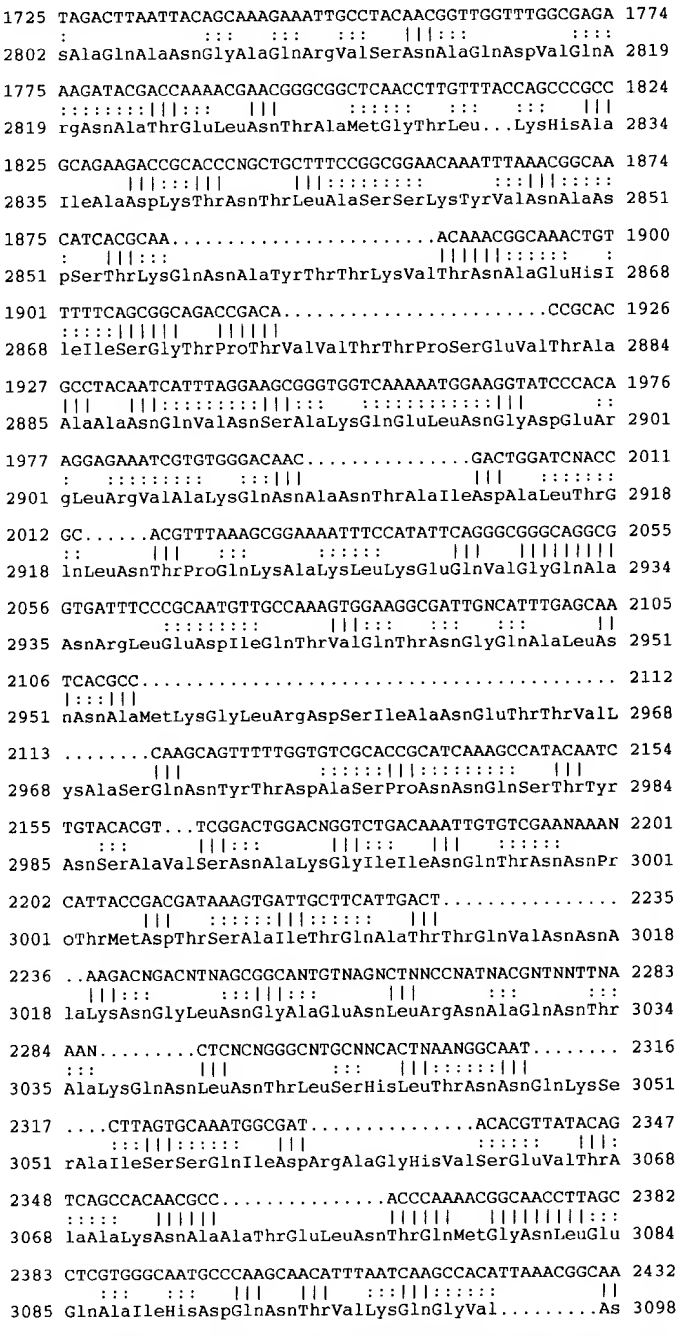


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2585 AAAACAGCCGCTTTACCGGACAACTCAGCGGCAGCAAGGANACAGCATTA 2634
3165 euAsnAsn......LeuThrSerIleAsnAsnAlaGlnLysArgAspLeu 3179
2635 CACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAA..... 2676
3180 ThrThrLysIleAspGlnAlaThrThrValAlaGlyValGluAlaValSe 3196
2677 .....TTAGGCAATTTA......AACC 2692
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2743 GGC.....GCGCAAACCGGCAGNGTGTCAGACACGCCGCGCCG 2780
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3246 eLeuAsnLysAsnSer...GlySerAsnLeuAspLysAlaAlaValGluA 3262
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3329 AsnGlyAlaMetGlyThrLeuArgAsn.....SerIleGlnAspAs 3342
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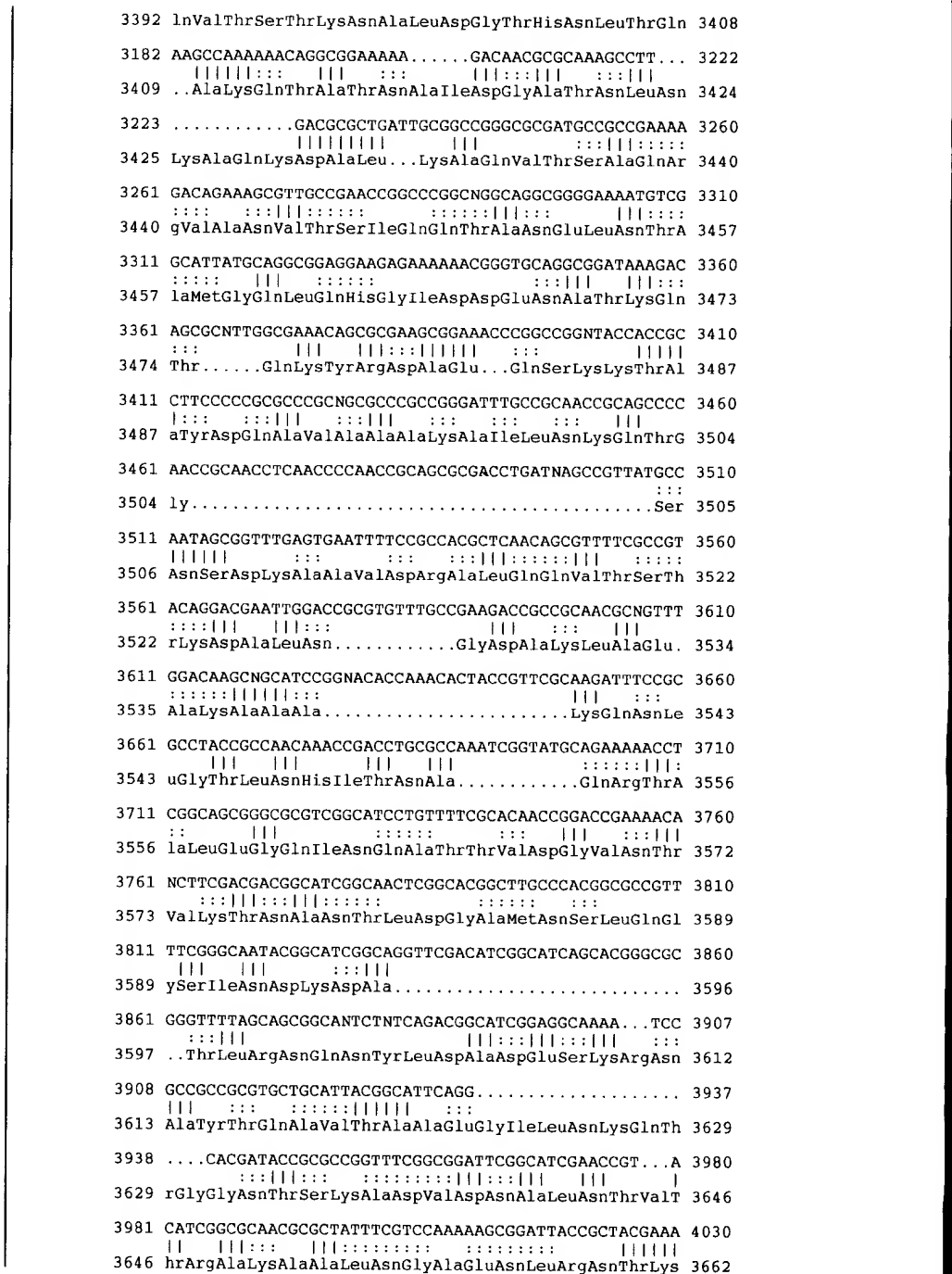
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3938 ....CACGATACCGCGCCGGTTTCGGCGGATTCGGCATCGAACCGT...A 3980
3629 rGlyGlyAsnThrSerLysAlaAspValAspAsnAlaLeuAsnThrValT 3646
3981 CATCGGCGCAACGCGCTATTTCGTCCAAAAAGCGGATTACCGCTACGAAA 4030
3646 hrArgAlaLysAlaAlaLeuAsnGlyAlaGluAsnLeuArgAsnThrLys 3662

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seq_documentation_block:

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AC   AAB01842;
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DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain 15 HMW1A protein, SEQ ID NO:59.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain 15.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52191.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 12; Fig 26A-O; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
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 618 ysAlaGluIleThrAlaLysAspGly..................... 626

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 627 ..............SerAspLeuThrIleGlyAsnThrAsnSer..... 636

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3224 ACGCGCTGATTGCGGCCGGG..............CGCGATGCCGCCGAA 3258
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 685 aGlyLeuThrIleAlaAlaLysAsnValGluValLysAsnAsnIleThrS 702

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 817 rLeuThrThrValGluGlySerAsnIleAsnAlaAlaSerGlyThrLeuV 834

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XX
AC AAB01841;
XX
DT 11-SEP-2000 (first entry)
XX
DE Haemophilus influenzae strain PMH1 mature HMW2A protein, SEQ ID NO:57.
XX
KW Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW recombinant production; Escherichia coli; antibacterial; vaccine;
KW human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW detection; diagnosis.
XX
OS Haemophilus influenzae strain PMH1.
XX
PN WO200020609-A2.
XX
PD 13-APR-2000.
XX
PF 07-OCT-1999; 99WO-CA00938.
XX
PR 07-OCT-1998; 98US-0167568.
PR 08-DEC-1998; 98US-0206942.
XX
PA (CONN-) CONNAUGHT LAB LTD.
XX
PI Loosmore SM, Yang Y, Klein MH;
XX
DR WPI; 2000-303789/26.
DR N-PSDB; AAA52190.
XX
PT Nucleic acid molecule for producing recombinant high molecular weight
PT proteins of Haemophilus which are used as a vaccine to provide
PT protection against Haemophilus induced diseases in humans -
XX
PS Claim 8; Fig 25A-O; 307pp; English.
XX
CC The invention relates to the recombinant production of Haemophilus
CC influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC expression construct used to effect recombinant expression comprises a
CC promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC and the hmwB and hmwC genes encode accessory proteins which are
CC responsible for post-translational processing and secretion of the HMWA
CC proteins. The modified hmwABC operon used in the expression construct of
CC the invention contains an A gene modified such that it encodes only the
CC mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC vectors are used for the production of recombinant H. influenzae HMW
CC proteins which can be used as vaccines to mediate a humoral or
CC cell-mediated immune response to provide protection against diseases in
CC humans caused by H. influenzae (e.g., otitis media, epiglottitis,

```
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   1004 AA;


alignment_scores:
           Quality:  240.00              Length:   1056
             Ratio:  0.481                Gaps:     47
 Percent Similarity:  47.254   Percent Identity: 21.023

alignment_block:
 US-09-303-518D-651 x AAB01841   ..

 Align seg 1/1  to: AAB01841  from: 1  to: 1004

    1369 ACGCTGCACGTTCAAGCCAAAGGGGAAAACCAAGGCTCGATCAGCGTGGG 1418
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       5 ThrIleAlaAlaGlyAlaProGlyArgAsnAspGlySerVal........ 18

    1419 CGACGGTACAGTCATTTTGGATCAGCAGGCAGACGATAAAGGCAAAAAAC 1468
                                      ||||||
      19 ..............................AspAsp.............. 20

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                           :::   :::|||||||||
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    1519 AATGCCGATAATCAGTTCAACCCCGACAAACTCTATTTCGGCTTTCGCGG 1568
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         |||   |||:::||||||:::::::::::::||||||      |||
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    1716 GAATATC..........................AATAGACTTAATTACA 1738
          ||||||                         ::::::   |||   :
      72 eAsnIleLysGlyGlyAlaHisLeuThrLeuTyrSerLysAsnAsnLysL 89

    1739 GCAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACCAAA 1788
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      89 ysSerSerValLysIleAsnGly............AsnIleThrSerThr 101

    1789 ACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCAC 1838
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     107 rIleTyrSerSerGlyTrpValAspIleHisLysAsnIleThrLeuAsnT 124

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     124 hrGlyTyrLeuAsnIleThrAlaGlyGlySerValAlaPheGluLysAla 140

    1930 TACAATCATTTAGGAAGCGGGTGGTCAAAAATGGAAGGTATCCCACAAGG 1979
            |||:::   |||         |||:::                |||||
     141 GlyAsnGluLysGlyArgGlnValSerGluSerValIleLysAlaGlnGl 157

    1980 AGAAATCGTGTGGGACAACGACTGGATCNACCGCACGTTTAAAGCGGAAA 2029
         |   |||          ::::::   :::   :::   |||:::   :::|
      157 yValIle.........ThrSerGlyValGlyGluGlyPheArgPheAsnA 171

    2030 ATTTCCATATTCAGGGC.......................GGGCAGGCG 2055
         ||      ::::::|||                              ||||||
      171 snValSerLeuAsnGlyValGlyAlaGlyLeuArgPheValGlyGlnLys 187

    2056 GTGATTTCCCGCAAT.....................GTTGCCAAAGTGGA 2084
            ||||||   |||                              :::   ::
      188 AsnIleSerSerAsnSerTrpArgGluAsnThrIleLysAsnArgPheAs 204

    2085 AGGCGATTGNCATTTGAGCAATCACGCCCAAGCAGTTTTTGGTGTCGCAC 2134
         :|||:::   ::::::|||:::   :::::::::   :::   |||:::
      204 pGlyAsnLeuAsnIleSerGlyLysValAsnValSerMetAspValSerG 221

    2135 CGCATCAAAGCCATACA...ATCTGTACACGTTCGGACTGGACNGGTCTG 2181
               :::   ||||||   |||      |||:::   |||:::
      221 lyThrLysTrpHisThrArgIleAsnGlyArgThrTyrTrpAsnValThr 237

    2182 ACAAATTGTGTCGAANAAANCATTACC..............GACGATAA 2216
         |||      |||   :::      :::                |||   ::
      238 ThrLeuAsnValAlaSerGlySerSerPheAsnLeuSerIleAspAlaSe 254

    2217 AGTGATTGCTTCATTGACTAAGACNGACNTNAGCGGCANTGTNAGNCTNN 2266
         :   |||:::|||   ::::::   |||   ::::::
      254 rGlyIleSerSerGlyAsnGlnAspAspIleThrAsn.............. 266

    2267 CCNATNACGNTNNTTNAAANCTCNCNGGGCNTGCNNCACTNAANGGCAAT 2316
                                                 |||   |||
      267 ..............................ArgGlyLeuAsnGly... 271

    2317 CTTAGTGCAAATGGCGATACACGTTATACAGTCAGCCACAACGCCACCCA 2366
         ::::::   ||||||::::::   ::::::::::::::::::::::|||
      272 IleThrPheAsnGlyGluAsnThrPheAsnIleAlaGlnGlySerThrAl 288

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    2407 TTTAATCAAGCCACATTAAACGGCAACNCATCGGNTTCGGGC........ 2448
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      338 eAsnSerGlnAsnPheAsnValSerGlyGlySerLysLeuAsnLeuLysA 355

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    2606 AA......CTCAGCGGCAGCAAGGANACAGCATTACACTTAAAAGACAGC 2649
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    2650 GAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTGACAA 2699
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    2700 CGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCTGCAGGCGCGC 2749
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 429 nAlaThrLeuArgSerAlaAsnPheAspAsnHisLysGlyAlaLeuIleV 446

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 446 alAsnGly..................................... 448

2800 TTATCCGTTACACCGCCAACTTCGGTAGAATCCCGTTTCAACACGCTGAC 2849
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2850 GGTAAACGGCAAATTGAAC...NGTCAAGGAACATTCCGCTTTATGTCGG 2896
       :::::::|||:::|||:::   :::||||||                ::::
 464 sIleLysGlyAsnLeuAspValAlaGlnGly.............AlaL 476

2897 AACTCTTCGGCTACCGAAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAA 2946
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 476 ysPheAsnGlySerThrLysAsnAsnLeuAsnIleThr.....;... 488

2947 GGNACTTACACCTTGGCGGTCAACAATACCGGCAACGAACCCGTAAGCCT 2996
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 489 GlyThrPheThr...........AsnAsnGlyThrSerIleIleAspIl 501

2997 CGATCAATTGACGGTAGTGGAAGGGAAAGACAACAAACCGCTGTCCGAAA 3046
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 501 eThrGlnGlyValValAsnLeuGly......AsnValThrAsnAspGlyL 516

3047 ACCTTAATTTCACCCTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGT 3096
     ::|||||:::|||   :::   :::      :::   :::      |||
 516 ysLeuAsnIleThrThrHisAlaLysSerGlyGlnLysSerIleIleArg 532

3097 TACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTG......CATAATCC 3140
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 533 GlyAspIleIleAsnLysGlnGlyAsnLeuAsnIleThrAspAsnAsnSe 549

3141 GGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAGAAGCCAAAA 3190
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 549 rAsnAlaGluIleGluIleGlyGlyAsnIleSerGlnLysGluGlyAsnL 566

3191 AACAGGCGGAAAAAGACAACGCGCAA...AGCCTTGACGCGCTGATTGCG 3237
               :::::::|||:::::::::   :::   :::      |||
 566 euThrIleSerSerAspLysValAsnIleThrLysGlnIleThrIleLys 582

3238 GCCGGGCGCGATGCCGCCGAAAAGACAGAAAGCGTTGCCGAACCGGCCCG 3287
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3288 GCNGGCA.....................................G 3295
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 599 nLeuThrIleLysThrLysGluLeuThrPheThrAspAsnLeuAsnIleS 616

3296 GCGGGGAAAATGTCGGCATTATGCAGGCGGAGGAAGAGAAAAAACGGGTG 3345
     ::|||   |||   :::   :::   |||:::::::::::::      :::
 616 erGlyPheAsnLysAlaGluIleThrAlaLysAspAsnSerAspLeuIle 632

3346 ......CAGGCGGATAAAGACAGCGCNTTGGCGAAACAGCGCGAAGCGGA 3389
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 633 IleGlyLysAlaSerSerAspAsnSerAsnAlaLysGln........... 645

3390 AACCCGGCCGGNTACCACCGCCTTCCCCCGCGCCCGCNGCGCCCGCCGGG 3439
                     ::::::|||   :::::::::   ::::::
 646 ..............ValThrPheAspLysValLysAspSerLys.... 655

3440 ATTTGCCGCAACCGCAGCCCCAACCGCAACCTCAACCCCAACCGCAGCGC 3489

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3490 GACCTGATNAGCCGTTATGCCAATAGCGGTTTGAGTGAATTTTCCGCCAC 3539
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 688 lyLeuThrIleSerAlaLysAsp..............ValThrValAsn 699

3622 ATCCGGNACACCAAACACTACCGTTCGCAAGATTTCCGCG.......... 3661
       :::   |||:::|||    :::   :::|||||||||
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3662 ...................CCTACCGCCAACAAACCGACCTGCGCCAAA 3691
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3727 GGCATCCTGTTTTCGCACAACCGGACCGAAAACANCTTCGACGACGGCAT 3776
     ::::|||         :::||||||      |||         :::|||:
 749 rValSerValThrAlaSerThrGlyAspLeuThrValArgLysAlaAlaT 766

3777 CG...GCAACTCGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAAT... 3820
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3821 ...ACGGCATCGGCAGGTTCGACATCGGCATCAGCACGGGCGCGGGTTTT 3867
        |||:::::|||||||||:::   :::|||:::::::::::|||
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3929 .........................GCATTCAGGCACGATACCGCGCC 3951
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 831 AsnIleLysAlaThrSerGlyThrLeuAlaIleAsnAlaLysAspAlaLy 847

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       :::::::::   :::::::::|||||||||:::::::::   :::   :
 847 sLeuAspGlyThrAlaSerGlyAsnArgThrGluValAsnAlaThrAsnA 864

4002 CGTCCAAAAAGCGGATTACCGCTACGAAAACGTCAATATCGCCACCCCCG 4051
     ::|||   :::      :::::::::|||||||||   |||
 864 laSerGlySerGlySerValThrAlaLysThrSer...SerAsnValAsn 879

4052 GTCTTGCGTTCAACCGNTACCGNGCGGGCATTAAGGCAGATTATTCATTC 4101
       :::      :::   :::|||   ::::::|||   :::||||||   ::
 880 IleThrGlyAspLeuSerThrIleAsnGlyLeu...AsnIleIleSerGl 895

4102 AAACCGGCGCAACACA 4117
     :|||   |||||||||
 895 uAsnGlyArgAsnThr 900
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01840

seq_documentation_block:
ID AAB01840 standard; Protein; 1010 AA.
XX
AC AAB01840;
XX
DT 11-SEP-2000 (first entry)
XX
DE Haemophilus influenzae strain PMH1 HMW2A protein, SEQ ID NO:55.
XX
KW HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW recombinant production; Escherichia coli; antibacterial; vaccine;
KW human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;

```
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain PMH1.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52189.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 12; Fig 25A-O; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
XX
SQ   Sequence   1010 AA;


alignment_scores:
            Quality:  240.00              Length:   1056
              Ratio:  0.481                 Gaps:     47
 Percent Similarity:  47.254   Percent Identity: 21.023

alignment_block:
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 Align seg 1/1  to: AAB01840  from: 1  to: 1010

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         |||:::   :::   |||   |||:::|||:::|||||||:::
      11 ThrIleAlaAlaGlyAlaProGlyArgAsnAspGlySerVal..... 24

    1419 CGACGGTACAGTCATTTTGGATCAGCAGGCAGACGATAAAGGCAAAAAAC 1468
                                  ||||||
      25 ..............................AspAsp............ 26

    1469 AAGCCTTTAGTGAAATCGGCTTGNTCAGCGGCAGGGGTACGGTGCAACTG 1518
                              :::   :::|||||||||
      27 .................PhePheProThrGlyArgGlyAspAspAlaSer 37

    1519 AATGCCGATAATCAGTTCAACCCCGACAAACTCTATTTCGGCTTTCGCGG 1568
         ||||||   ::::::   :::|||||||||
      38 AsnAlaLysThrAsn...HisProAspLys..................... 46

    1569 CGGACGTTTGGATTTAAACGGGCATTCGCTTTCGTTCCACCGTATTCAAA 1618
                                                      :::   |
      47 ....................................ProThrLeuThrA 51

    1619 ATACCGATGAAGGGGCGATGATTGNCNATCATAATGCCACAACAACATCC 1668
         |||||                  :::   :::||||||     .::::::
      51 snThr.................ThrValGluAsnAlaLeuLysAsnAsn 61

    1669 ACC...GTTACCATTACAGGGAATGAAAGTATTACACAACCGAGTGGTAA 1715
         |||   |||:::||||||:::::::::::::||||||      |||
      62 ThrPheValAsnIleThrAlaLysAsnLysIleThrValAsnSerAspIl 78

    1716 GAATATC.........................AATAGACTTAATTACA 1738
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      78 eAsnIleLysGlyGlyAlaHisLeuThrLeuTyrSerLysAsnAsnLysL 95

    1739 GCAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACCAAA 1788
         ::::::::::      ||||||          :::   |||:::
      95 ysSerSerValLysIleAsnGly.....AsnIleThrSerThr 107

    1789 ACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCAC 1838
         |||||||||:::|||                                ||
     108 ThrAsnGlyAsnLeu.............................Th 113

    1839 CCNGCTGCTTTCCGGCGGAACAAATTTAAACGGCAACATCACGCAAACAA 1888
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     113 rIleTyrSerSerGlyTrpValAspIleHisLysAsnIleThrLeuAsnT 130

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     177 snValSerLeuAsnGlyValGlyAlaGlyLeuArgPheValGlyGlnLys 193

    2056 GTGATTTCCCGCAAT.....................GTTGCCAAAGTGGA 2084
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     194 AsnIleSerSerAsnSerTrpArgGluAsnThrIleLysAsnArgPheAs 210

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    2182 ACAAATTGTGTCGAANAAANCATTACC..............GACGATAA 2216
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    2217 AGTGATTGCTTCATTGACTAAGACNGACNTNAGCGGCANTGTNAGNCTNN 2266
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     260 rGlyIleSerSerGlyAsnGlnAspAspIleThrAsn.............. 272
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AC AAG98256;
XX
DT 21-SEP-2001 (first entry)
XX
DE Escherichia coli protein sequence SEQ ID NO:304.
XX
KW Escherichia coli; identification; proliferation; microorganism;
KW antimicrobial; antibacterial; antibiotic; gene therapy; diagnosis;
KW bacterial growth inhibition.
XX
OS Escherichia coli.
XX
PN WO200148209-A2.
XX
PD 05-JUL-2001.
XX
PF 19-DEC-2000; 2000WO-US34419.
XX
PR 23-DEC-1999; 99US-0173005.
XX
PA (ELIT-) ELITRA PHARM INC.
XX
PI Forsyth RA, Ohlsen KL, Zyskind JW;
XX
DR WPI; 2001-457376/49.
DR N-PSDB; AAH81312.
XX
PT Novel nucleic acids encoding proteins required for Escherichia coli
PT proliferation, useful for screening for antimicrobial agents -
XX
PS Claim 19; Page 445-448; 596pp; English.
XX
CC The present invention describes a purified or isolated nucleic acid
CC sequence (I) consisting essentially of one of the 93 nucleotide sequences
CC given in AAH81202 to AAH81294, where expression of the nucleic acid in a
CC microorganism is capable of inhibiting proliferation of a microorganism.
CC (I) have antibacterial and antibiotic activities, and can be used in
CC gene therapy. Expression of (I) in a microorganism inhibits proliferation
CC of the microorganism, and the manufactured antibiotic is useful for
CC reducing the activity or level of a gene product required for
CC proliferation of a microorganism in a subject, specifically humans. The
CC nucleic acids that inhibit bacterial growth or proliferation can be used
CC as antisense therapeutics for killing bacteria. In addition to
CC therapeutic applications, the nucleic acid sequences complementary to
CC sequences required for proliferation can be used as diagnostic tools.
CC For example, nucleic acid probes complementary to proliferation-required
CC sequences that are specific for particular species of microorganisms can
CC be used as probes to identify particular microorganism species in
CC clinical specimens. AAH81295 to AAH81487 encode the Escherichia coli
CC proteins given in AAG98239 to AAG98431, and AAH81488 to AAH81491
CC represent oligonucleotides, which are used in the exemplification of the
CC present invention.
XX
SQ Sequence 1325 AA;

alignment_scores:

Quality:	236.00	Length:	961
Ratio:	0.524	Gaps:	50
Percent Similarity:	46.826	Percent Identity:	20.604

alignment_block:
US-09-303-518D-651 x AAG98256 ..

Align seg 1/1 to: AAG98256 from: 1 to: 1325

```
 634 GATTTATCCTACTCCGGCGCATGGTTAATTGGC.............GGCAA 671
     |||::::::|||:::   |||:::|||:::|||              |||
  77 AspValAlaTyrAsp...AlaTyrLeuValGlyTrpTyrGlyThrGlyVa 92

 672 TACACATATGCAGGGTTGGGGAAATAATGGCGTANTTAGTTTGAGCGGCG 721
         ::::::   :::   ||||||   :::::::::::::::::   :
  92 lLeuAsnIleLeuAlaGlyGlyAsnAlaSerLeuThrThrIleThrThrS 109

 722 ATGTGCGCCATGCCAACGACTATGGCCCTATGCCGATTGCAGGTGCGGCA 771
     ::|||      ||||||:::                    |||:::::::
 109 erValIleGlyAlaAsnGlu.............AspSerGluGlyThrVal 121

 772 GGCGACAGCGGTTCGCCAATGTTTATTTATGACAAAACAAACAATAAATG 821
     :::      |||:::      :::|||||||:::   ||||||
 122 AsnValLeuGlyGlyThrTrpArgLeuTyrAspSerGlyAsnAsnAlaAr 138

 822 GCTGCTCAACGGAGTTTTACAAACCGGCTACCCTTATTCCGGCAGGGAAA 871
         ||||||   |||   |||:::|||
 138 gProLeuAsn...ValGlyGlnSerGly..................... 146

 872 ACGGTTTCCAGCTGATACGCAAAGATTGGTTCTACGATGACATTTACAGA 921

 146 ................................................. 146

 922 GGCGATACACATACCGTCTNTTTTGAACCGCGCAGTAAC.........GG 962
           |||   |||:::   ::::::   :::::::::         ||
 147 ......ThrGlyThrLeuAsnIleLysGlnLysGlyHisValAspGlyGl 161

 963 ACATTTTTCCTTTACATCCAACAACAACGGTACGGGTACGGTAACAGAAA 1012
     |::::::   :::   |||:::::::::|||:::|||||||||:::
 161 yTyrLeuArgLeuGlySerSerThrGlyGlyValGlyThrValAsnValG 178

1013 CCAACGAAAAGGTNTCCAATCCAAAGCTTAAAGTACAGACAGTCCGACTG 1062
       :::|||                    :::|||   |||::::::|||
 178 luGlyGluAsp.................SerValLeuThrThrGluLeu 188

1063 TTTGAC.................GAATCTTTGAATGAAACTGATAAAGA 1094
     |||:::                 |||||||||   |||||||||
 189 PheGluIleGlySerTyrGlyThrGlySerLeuAsnIleThrAspLysGl 205

1095 ACCAGTT.........................TACGCGGCAGGGGGTG 1117
         |||                       |||   ||||||
 205 yTyrValThrSerSerIleValAlaIleLeuGlyTyrGlnAlaGly.... 220

1118 TTAATCAGTACCGTCCAAGGTTAAACAACGGTGAAAACCTTTCTTTTATC 1167
```

```
 2680 GGCAATTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCTATCG 2729
      |||:::      ::::::::::::   :::|||:::   |||
  717 GlyLysThrLeuValAsnAspGlyLeuLeuThrIleAlaSer...,..... 730

 2730 CCACGATGCTGCAGGCGCGCAAACCGGCAGNGTGTCAGACACGCCGCGCC 2779
       |||   |||   |||:::   ||||||      |||
  731 .HisThrAlaAspGlyVal...ThrGlyMetGlySer.....!..... 741

 2780 GCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAA 2829
                  |||   ::::::::::::   |||
  742 .............SerGluValThrIleAlaAsnPro.....'..... 749

 2830 TCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACNGTCAAGGAAC 2879
             :::||||||   :::   ::::::   |||:::   |||
  750 .........GlyThrLeuAspIleLeuAlaSerThrAsnSerAlaGlyAs 763

 2880 ATTCCGCTTTATGTCGGAACTCTTCGGCTACCGAAGCGACAAATTGAAGC 2929
       :::   :::   :::   |||   |||             :::::::::|
  763 pTyrThrLeuThrAsnAlaLeuLysGlyAspGlyLeuMetArgValGlnL 780

 2930 TGGCGGAAAGTTCCGAA...GGNACTTACACCTTGGCGGTCAACAATACC 2976
      ||:::::::|||::::::         :::|||   |||         |||
  780 euSerSerSerAspLysMetPheGlyPheThrHisAla.........Thr 793

 2977 GGCAACGAACCCGTAAGCCTCGATCAATTGACGGTAGTGGAAGGGAAAGA 3026
      |||:::|||   :::::::::   ||||||               |||||
  794 GlyThrGluPheAlaGlyValAlaGlnLeu..............LysAs 805

 3027 CAACAAACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAACACG 3076
      |:::                     :::||||||||||:::::::::
  805 pSer.....................ThrPheThrLeuGluArgAsp.... 813

 3077 TCGATGCCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTC 3126
        :::::::::|||      :::   ::::::::::::|||:::|||
  814 ..AsnThrAlaAlaLeuThrHisAlaMetLeuGlnSerAspSerGluAsn 829

 3127 CGCCTGCATAATCCGGTCAAAGAACAAGAGCTT 3159
                   |||   ||||||::::::
  830 ThrThrSerValLysValGlyGluGlnSerIle 840
```

seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01843

seq_documentation_block:

ID AAB01843 standard; Protein; 992 AA.
XX
AC AAB01843;
XX
DT 11-SEP-2000 (first entry)
XX
DE Haemophilus influenzae strain 15 mature HMW1A protein, SEQ ID NO:61.
XX
KW Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW recombinant production; Escherichia coli; antibacterial; vaccine;
KW human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW detection; diagnosis.
XX
OS Haemophilus influenzae strain 15.
XX
PN WO200020609-A2.
XX
PD 13-APR-2000.
XX
PF 07-OCT-1999; 99WO-CA00938.
XX
PR 07-OCT-1998; 98US-0167568.
PR 08-DEC-1998; 98US-0206942.
XX
PA (CONN-) CONNAUGHT LAB LTD.
XX
PI Loosmore SM, Yang Y, Klein MH;
XX
DR WPI; 2000-303789/26.
DR N-PSDB; AAA52192.
XX
PT Nucleic acid molecule for producing recombinant high molecular weight
PT proteins of Haemophilus which are used as a vaccine to provide
PT protection against Haemophilus induced diseases in humans -
XX
PS Claim 8; Fig 26A-O; 307pp; English.
XX
CC The invention relates to the recombinant production of Haemophilus
CC influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC expression construct used to effect recombinant expression comprises a
CC promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC and the hmwB and hmwC genes encode accessory proteins which are
CC responsible for post-translational processing and secretion of the HMWA
CC proteins. The modified hmwABC operon used in the expression construct of
CC the invention contains an A gene modified such that it encodes only the
CC mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC vectors are used for the production of recombinant H. influenzae HMW
CC proteins which can be used as vaccines to mediate a humoral or
CC cell-mediated immune response to provide protection against diseases in
CC humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC antigens in immunoassays for detecting antibodies against Haemophilus,
CC HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC HMW proteins can be used to isolate and clone hmw genes from other
CC non-typeable strains of Haemophilus via hybridisation reactions. The
CC present sequence represents a mature HMWA protein from a non-typeable
CC strain of H. influenzae.
XX
SQ Sequence 992 AA;

alignment_scores:

```
            Quality:  232.50              Length:   1123
              Ratio:  0.454                 Gaps:     56
 Percent Similarity:  45.592   Percent Identity: 19.768
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alignment_block:

US-09-303-518D-651 x AAB01843 ..

Align seg 1/1 to: AAB01843 from: 1 to: 992

```
  691 GGAAATAATGGCGTANTTAGTTTGAGCGGCGATGTGCGCCATGCCAACGA 740
      ||||||   |||:::   |||
   14 GlyAsnAlaGlyIleAspSer............................. 20

  741 CTATGGCCCTATGCCGATTGCAGGTGCGGCAGGCGACAGCGGTTCGCCAA 790
                     :::   |||:::::|||   :::   ||||||
   21 .............GluPheProGlyGlySerGlyThrLysGluSerPro. 32

  791 TGTTTATTTATGACAAAACAAACAATAAA..................... 819
                  |||||||||::::::
   33 .............LysThrAsnGlyGluGlnProThrValLeuThrAsn 44

  820 ................................TGGCTGCTCAACGGAGT 836
                                      |||::::::|||   ::
   45 GluThrIleSerAsnTyrLeuLysSerGlyThrTrpValMetAsnIleTh 61

  837 TTTACAAACCGGCTACCCTTATTCC........................ 861
      :   :::   :::         :::
   61 rAlaLysLysAsnLeuThrValAsnSerSerIleAsnIleGlyAspSerS 78

  862 ......................GGCAGGGAAAACGGTTTCCAGCTGATA 888
                             |||::::::||||||         |||
   78 erHisLeuIleLeuHisSerGluGlyLysAsnAsnGlyGlyValLysIle 94
```

```
 615 IleThrAlaLys.............................AspGl 620

2295 GCNTGCNNCACTNAANGGCAATCTT...AGTGCAAATGGCGATACACGTT 2341
     |:::           ||||||      ||||||::::::   :::
 620 ySerAspLeuThrIleGlyAsnThrAsnSerAlaAspSerThrAsnAlaL 637

2342 ATACAGTCAGCCACAACGCCACCCAAAACGGCAACCTTAGCCTCGTGGGC 2391
       |||:::   |||   :::::::::::::::::::|||   :::|||
 637 ysLysValThrPheAsnGlnValLysAspSerLysIleSer...AlaGly 652

2392 AATGCCCAAGCAACATTTAAT...CAAGCCACATTAAACGGCAACNCATC 2438
     :::   ::::::|||:::|||   ::::::      :::||||||:::::
 653 AspHisAsnValThrLeuAsnSerLysValGluThrSerGlyAsnThrAs 669

2439 GGNTTCGGGCAATGCTTCATTTAAT..................... 2463
     :   :::|||::::::|||   |||
 669 pAsnThrGlyAspGlySerGlyAsnAsnAlaGlyLeuThrIleAlaAlaL 686

2464 ..........CTAAGCAACAACGCCGCACAAAACGGCAGTCTGACGCTT 2502
             :::::::||||||   :::::::|||   ::::::::::::
 686 ysAsnValGluValLysAsnAsnIleThrSerAsnLysThrValAsnIle 702

2503 TCCGACAAC...........GCTAAGGCAAACGTAAGCCATTCCGCACT 2540
     :::   :::           :::||||||:::::::::   :::|||
 703 ThrAlaSerGluLysLeuThrThrLysAlaAspAlaThrIleAsnAlaTh 719

2541 CAACGGCAATGTCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAACA 2590
      :::||||||||||:::::::::   |||
 719 rThrGlyAsnValGluValThrAlaLys..................... 728

2591 GCCGCTTTACCGGACAACTCAGCGGCAGC...AAGGANACAGCATTACAC 2637
           ||||||::::::::::|||:::   |||:::|||:::
 729 ........ThrGlyAspIleLysGlyGluValLysSerThrSer...... 740

2638 TTAAAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTT 2687
                                                ||||||::
 741 ....................................GlyAsnVa 743

2688 AAACCTTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGATG 2737
     :|||:::                |||||||||   :::         :::::
 743 lAsnIleThrAlaAsnGlyAspThrLeuAsnValSer.........AsnV 757

2738 CTGCAGGCGCGCAAACCGGCAGNGTGTCAGACACGCCGCGC......CGC 2781
     ::::::|||      :::      :::::::|||      :::
 757 alSerGlyAsnAlaValThrIleThrAlaAspLysGlyLysLeuThrThr 773

2782 CGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAATC 2831
     ::::::      |||:::   |||   :::      |||::::::   :::
 774 GlnAlaSerSerSerIleThrSerAsnAsnGlyGlnThrThrLeuThrAl 790

2832 CCGTTTCAACACGCTG..............ACGGTAAACGGCAAATTGA 2866
     ::::   :::::::::             ::::::|||      ||||
 790 aLysAspGlySerIleAlaGlySerIleAsnAlaAlaAsnValThrLeuA 807

2867 ACNGTCAAGGAACATTCCGCTTTATG.....................:.... 2892
     ||:::   ||||||:::      :::
 807 snThrThrGlyThrLeuThrThrValGluGlySerAsnIleAsnAlaAla 823

2893 ......TCGGAACTCTTCGGCTACCGAAGCGACAAATTGAAGCTGGCGGA 2936
           :::   :::::::::   ::::::   ||||||:::   |||
 824 SerGlyThrLeuValIleAsnAlaLysAspAlaLysLeuAsnGlyAlaAl 840

2937 AAGTTCCGAAGGNACTTACACCTTGGCGGTCAACAATACCGGCAACGAAC 2986
      |||::::::   |||   :::   |||:::|||   :::||||:::
 840 aSerGlyAspHisThrValValAsnAlaThrAsnAlaSerGlySer.... 855

2987 CCGTAAGCCTCGATCAATTGACGGTAGTGGAAGGGAAAGACAACAAACCG 3036
                                       |||:::   :::
 856 ..............................GlySerValThrAlaVal 861

3037 CTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGATGCCGG 3086
        |||:::|||:::|||:::|||   :::   :::   |||::::::
 862 ThrSerSerAsnValAsnIleThrGlyAspLeuSerThrValAsnGly.. 877

3087 CGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGCATA 3136
                    ::::::|||   |||:::|||            :::|
 878 ..........LeuAsnIleIleSerLysAsnGly............ArgA 887

3137 ATCCGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAGAAGCC 3186
     ||   |||                                |||       :::|||
 887 snThrVal.....................ValLeuLysGlyThrGluIle 896

3187 AAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTGACGCGCTGATTGC 3236
     :::   :::      :::   ::::::   |||:::::::   :::|||
 897 GluValLysTyrIleGlnProGlyValAlaSerValGluGluValIleGl 913

3237 GGCCGGGCGCGATGCCGCCGAAAAGACAGAAAGCGTTGCCGAACCGGCCC 3286
      |||   |||   :::   ||||||:::::::::::::::::::      |
 913 uAlaLysArg...ValLeuGluLysValLysAspLeuSerAspGluGluA 929

3287 GGCNGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCGGAGGAAGAGAAA 3336
     ||   :::   ::::::   :::|||:::      :::
 929 rgGluThrLeuAlaLys...LeuGlyValSerAlaVal............ 940

3337 AAACGGGTGCAGGCGGATAAAGACAGCGCNTTGGCGAAACAGCGCGAAGC 3386
     :::   ::::::   ::::::      ::::::      |||:::|||
 941 ArgPheIleGluProAsnAsnThrIleThrValAsnThrGlnAsnGluPh 957

3387 GGAAACCCGGCCGGNTACC 3405
          |||||||||::::::
 957 eThrThrArgProSerSer 963
```

seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:AAB59826

seq_documentation_block:

ID AAB59826 standard; Protein; 1615 AA.
XX
AC AAB59826;
XX
DT 04-APR-2001 (first entry)
XX
DE Protein #3 encoded by TutD/E gene.
XX
KW Toluene degradation; enzyme; waste degradation; TutE; TutD.
XX
OS Thauera aromatica.
OS Xanthomonas maltophilia.
OS Geobacter metallireducens.
OS Azoarcus tolulyticus.
XX
PN WO200072650-A2.
XX
PD 07-DEC-2000.
XX
PF 24-MAY-2000; 2000WO-US14298.
XX
PR 01-JUN-1999; 99US-0323872.
XX
PA (UYOH-) UNIV OHIO.
XX
PI Coschigano PW;
XX
DR WPI; 2001-041080/05.
DR N-PSDB; AAF23627.
XX
PT Composition comprising toluene degrading enzyme useful for biological
PT treatment of organic compounds, especially for degrading toluene or its
PT analogs -
XX
PS Disclosure; Fig 12; 122pp; English.
XX
CC The present invention relates to toluene degrading enzyme genes and
CC proteins tutH (see AAF23629 and AAB59831), tutI (AAF23630 and AAB59832),
CC tutF (AAF23631 and AAB59833) and tutG (AAF23632 and AAB59834). The
CC toluene degrading enzymes are homologues of pyruvate formate lyase. The
CC toluene degrading enzymes are useful for biological treatment of organic

```
CC   compounds and in particular for the degradation of toluene and its
CC   analogs contained in liquid or solid waste source. The present sequence
CC   is a protein sequence encoded by toluene degrading enzyme gene, TutD/E.
XX
SQ   Sequence   1615 AA;


alignment_scores:
           Quality:  232.00            Length:    733
             Ratio:  0.701               Gaps:     43
 Percent Similarity:  45.157   Percent Identity: 23.738

alignment_block:
 US-09-303-518D-651 x AAB59826   ..

 Align seg 1/1  to: AAB59826  from: 1  to: 1615

    2582 TTGAAAACAGCCGCTTTACCGGACAACTCAGCGGCAGCAAGGANACAGCA 2631
          ||||||   |||:::   |||   :::||||||:::|||      :::||
     552 LeuLysArgAlaSerArgProAlaSerSerAlaCysAlaIleProLysHi 568

    2632 T.....TACACTT 2639
         |     ::::::
     568 sThrArgProAlaLysAlaAsnProLysProSerValAlaArgTrpAlaT 585

    2640 AAAAGACAGCGAATGGACGC......TGCCGTCAGGCACGGAATTAGGCA 2683
           :::|||::::::::::|||      |||   :::      |||   :::
     585 rpArgThrSerThrSerArgProTrpCysSerArgArgThrAsnSerSer 601

    2684 ATTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCAC 2733
               :::   |||||||||         :::|||||      ::: |
     602 ......SerAlaThrThrPro.........LysIleProThrCysSer.A 613

    2734 GATGC.....TGCAGGCGC 2747
         |||||          ||| |||||
     613 rgCysIleProAsnCysProThrTrpProCysArgThrThrCys.GlyAl 629

    2748 GCAAACCGGCAGNGTGTCAGACACGCCGCGCCGCCGTTCGCGCCGTTCCC 2797
         |   |||               |||   ||||||||||||   :::::
     629 aThrThrArgArgSerArgProThrArgArgArgArgSerMetAsnThrG 646

    2798 TATTATCCGTTACACCGCCAACTTCGGTAGAATCCCGTTTCAACACGCTG 2847
                :::::      :::||||||  :::|||:::|||
     646 lySerArgIleAlaCysArgAlaSerVal.SerProIleSer........ 659

    2848 ACGGTAAACGGCAAATTGAACNGTCAAGGAACATTCCGCTTTATGTCGGA 2897
                              :::::::::   ||||||   |||   :
     660 .....IleArgGlnThrSerAlaAlaCysIleA 669

    2898 ACTCTTCGGCTACCGAAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAG 2947
         ::|||:::|||                    ||||||:::
     669 rgSerAlaAla.....................TrpArgArg......... 675

    2948 GNACTTACACCTTGGCGGTCAACAATACCGGCAACGAACCCGTAAGCCTC 2997
                       |||   ::::::|||:::
     676 ..............ArgProSerLeuProVal.................. 681

    2998 GATCAATTGACGGTAGTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAA 3047
                                    ||||||     ||| |||
     682 ..........................ThrThrAlaSerCys.Arg... 687

    3048 CCTTAATTTCACCCTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTT 3097
                    |||:::|||   :::   ::: :::|||:::||||||
     688 ............ProThrLysProSerTrpLys.ThrGlyCysTrpArg. 699

    3098 ACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAA 3147
         ::::::||||||   |||:::   |||
     700 AlaSerSerSerProLysSerIleSerProLys.................. 710

    3148 GAACAAGAGCTTTCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGC 3197
                      |||      ::::::|||   :::|||   :::   |
     711 .............ProArgProThrCysArgProSerProSerProGlyThrAlaA 723

    3198 GGAAAAAGACAACGCGCAAAGCCTTGACGCGCTGATTGCGGCCGGGCGCG 3247
         ||:::   :::|||   :::                        |||   :::
     723 rgArgValSerThrThrSer.....................ProArgSer 732

    3248 ATGCCGCCGAAAAGACAGAAAGCGTTGCCGAACCGGCCCGGCNGGCAGGC 3297
                   :::|||   ::::::      :::|||   :::   :::||
     733 ThrThrGlyArgArgTrpSerSerProAlaArgArgSerAlaGlyArgAl 749

    3298 GGGGAAAATGTCGGCATTATGCAGGCGGAGGAAGAGAAAAAACGGGTGCA 3347
         ||||:::      |||   |||   |||   :::||||||::::::   |
     749 aGlyArg......AlaGlyCysAlaArgSerSerArgLysThrSer...A 763

    3348 GGCGGATAAAGACAGCGCNTTGGCGAAACAGCGCGAAGCGGAAACCCGGC 3397
         ||   |||::::::|||      |||   |||:::::::::::::|||
     763 rgProIleArgSerAla......ArgProSerCysSerLysSerProThr 777

    3398 CGGNTACCA......CCGCCTTCCCCCGCGCCCGCNGCGCCCGCCGGGAT 3441
                        ||||||||||||||||   |||:::   :::
     778 SerValSerAlaPheProProSerProAlaArgAlaSerArgThrArgCy 794

    3442 TTGCCGCAACCGCAGCCCCAAC......CGCAACCTCAACCCCAACCGCA 3485
               ||||||      |||:::         :::   :::   :::|||:
     794 sArgArgAsnSerLeuProSerSerValThrArgSerSerAlaThrArgA 811

    3486 GCGCGACCTGATNAGCCGTTATGCCAATAGCGGTTTGAGTGAATTTTCCG 3535
         ::||||||                |||   :::      ::::::   |||
     811 laAlaThrProArgArgLysThrProCysCysGlyArgThrThrArgPro 827

    3536 CCACGCTCAACAGCGTTTTCGCCGTACAGGACGAATTGG........... 3574
         |||   ||||||      |||      |||:::::::|||
     828 ProSerSerThrArgAsnSerSer...ArgAlaThrTrpMetArgTrpAs 843

    3574 ..................................................... 3574

     843 nSerSerArgTrpAsnValArgPheProSerMetAlaProAlaSerArgA 860

    3575 ..........................ACCGCGTGT......TTGCCG 3589
                                    |||   |||         |||
     860 laProThrAlaLysSerSerArgGlyArgThrIleCysSerSerSerPro 876

    3590 AAGACCGCCGCAACGCNGTTTGGACAAGCNGCATCCGGNACACCAAACAC 3639
         ::::::|||   |||      :::::::::   :::   ||||||:::
     877 SerAlaAlaProThrProArgAlaArgThrProAlaThrThrProThrPr 893

    3640 TACCGTTCGCAAGATTTCCGCGCCTACCGCCAACAAACCGACCTGCGCCA 3689
          :::   |||:::   |||:::   :::      :::|||      ::::
     893 oSerSerArgGlnProSerGlySerAlaArgProSerProProSerSerS 910

    3690 AATCGGTATGCAGAAAAACCTCG.........GCAGCGGGCGCGTCGGCA 3730
         ::::::::   |||:::|||:::         :::||||||   |||:::
     910 erAlaIleProArgArgThrAlaArgArgArgCysAlaGlyPheSerSer 926

    3731 TCCTGTTTTCGCACAACCGGACCGAAAACANCTTCGACGACGGCATCGGC 3780
         :::              ::::::   :::   :::|||||||||   |||||
     927 AlaSerAlaThrAspSerAlaIleArgArgSerSerThrThrArgSerAl 943

    3781 A...ACTCGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAATACGGCAT 3827
         |   :::|||::::::   |||:::         |||::::::||||||:
     943 aArgSerArgArgAsnThrProSer.........SerAlaSerThrAlaT 957

    3828 CGGCA.....................GGTTCGACATCGGCATCAGCA 3853
         ::|||                     |||||||||   :::::::::
     957 hrAlaProProThrArgLysProThrThrGlySerThrCysCysAlaCys 973

    3854 CGG...GCGCGGGTTTTAGCAGCGGCANTCTNTCAGACGGCATCGGAG.. 3898
         |||   |||  ::::::||||||         :::   :::   :::
     974 ArgProAlaSerThrValAlaAlaArgArgLysLysProValArgLysVa 990

    3899 ....GCAAAATCCGCCGCCGCGTGCTGCATTACGGCATTCAGGCACGATA 3944
             |||:::|||:::      |||      :::   |||      |
     990 lAlaAlaGlnSerSerArgProSerCysTrpLysSer...ArgSerMetT 1006

    3945 CCGCGCCGGTTTCGGCGGATTCGGCATCGAACCGTACATCGGCGCAACGC 3994
```

```
      |||||   ::::::         :::   |||      ||||||:::|||
1006 hrAlaThrThrGlyArgThrProThrCysAsn......SerAlaArgArg 1020

3995 GCTATTTCGTCCAAAAAG.....................CGGATTACCGC 4023
        :::   |||:::::                      |||:::::||
1021 ProValIleSerArgArgSerProSerArgMetPheGlyArgLeuSerAl 1037

4024 TACG..............AAAACGTCAATATCGCCACCCCCGGTCTTGC 4058
     |:::              :::||||||:::|||   |||   :::   |
1037 aSerSerIleAsnMetArgSerThrSerValSerAlaProArgThrCysA 1054

4059 GTTCAACCGNTACCGNGCGGGCATTAAGGCAGATTATTCATTCAAACCGG 4108
     ||:::|||:::::::::   :::   |||   :::      ||| |:
1054 rgAlaThrSerSerSerAlaSerCysArgCysLeu......SerCysPro 1068

4109 CGCAACACATNTCCATCACNCCTTATTTNAGCCTGTCCTATACCGATGCC 4158
     ::::::|||:::   :::                  |||   |||   ||
1069 GlnSerThrThrAlaAlaTrpAsnSerGlyTrpThrProAlaProCysPr 1085

4159 G.....................CTTCGGGCAAAGTCCGAACACGCGTCAA 4187
     |                      |||::::::   :::
1085 oSerSerProMetAlaGlyThrThrArgSerArgArgSerSerArgArgT 1102

4188 TACCGCNGTAT............TGGCTC..................... 4204
       |||::::::         |||
1102 hrProSerTrpProSerArgAsnTrpTyrSerArgArgArgAsnThrPro 1118

4205 ..............................AGGATTTCGGCAAAA.. 4219
                                    ::::::|||   |||
1119 SerSerAsnSerAlaLysArgArgArgThrGlyLysValSerArgLysCy 1135

4220 ..................................................C 4220
                                                       |
1135 sAlaSerThrSerSerGlyArgArgSerGlyAlaThrThrMetIleThrP 1152

4221 CCGCAGTGCGGAATGGGGCGTAAACGCCGAAATCAAAGGTTTCACGCTGT 4270
     ||:::|||   :::   |||   |||   ||||||:::::::::::::|||
1152 roThrValSerSerProAlaSerThrArgLysSerSerAlaAlaLysCys 1168

4271 .........CCNTCCACGCTGCCGCCGCCAAAGGNCCGC........... 4300
             |||:::||||||         :::   |||
1169 AlaArgSerProThrThrLeuValValArgSerCysArgLeuValArgLe 1185

4301 ..........AACTGGAAGCGCAACACAGCGCGGGCA 4327
               :::||||||         |||||||||
1185 uSerAlaCysThrTrpLysSerValArgAlaArgAla 1197
```

seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01834

seq_documentation_block:

```
ID   AAB01834 standard; Protein; 1101 AA.
XX
AC   AAB01834;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain LCDC2 HMW1A protein, SEQ ID NO:43.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain LCDC2.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52183.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 12; Fig 22A-P; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
XX
SQ   Sequence   1101 AA;
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alignment_scores:

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           Quality:  231.00              Length:   1008
             Ratio:  0.456                 Gaps:     55
 Percent Similarity:  50.298   Percent Identity: 21.329
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alignment_block:

US-09-303-518D-651 x AAB01834 ..

Align seg 1/1 to: AAB01834 from: 1 to: 1101

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  77 IleAsnIleLysGluAsnSerHisLeuIleLeuTrpSerGluArgAspGl 93

 601 CACTATTGGCGTTATGATGATGACAAACAC.............GGCG 634
      :::   ||||||::::::      |||                |||:
  93 yAsnSerGlyValGlnIleAspGlyAsnIleThrSerAlaThrGlyGlyS 110

 635 ATTTATCC...TACTCCGGCGCATGGTTAATTGGCGGCAATACACATATG 681
     ::|||:::   ||||||:::::::|||:::         ::::::|||
 110 erLeuThrValTyrSerSerGlyTrpVal.........AspValHisLys 123

 682 CAGGGTTGGGGAAATAATGGC.........GTANTTAGTTTGAGCGGCGA 722
     :::        |||:::|||          :::::::::   ||||||||
 124 AsnIleThrLeuAsnSerGlyTyrLeuAsnIleThrThrLysSerGlyAs 140

 723 TGTG......CGCCATGCCAACGACTATGGCCCTATGCCGATTGCAGGTG 766
     ||||      :::::::::||||||         :::   |||:::|||
```


140 pValAlaPheGluGlnGlyAsnAsp.....LeuThrIleThrGlyG 154
767 CGGCAGGCGACAGCGGTTCGCCAATG...TTTATTTATGACAAAACAAAC 813
154 lnGlyThrIleThrAlaSerLysLysGlyPheArgPheAspAsnValThr 170
814 AATAAATGGCTGCTCAACGGAGTTTTACAAACCGGCTACCCTTATTCCGG 863
171 LeuSerGlyValLysLysGlyPheLeu.....PheLysTyrSerGl 184
864 CAGGGAAAACGGTTTCCAGCTGATACGCAAAGATTGGTTCTACGATGACA 913
184 nThrAsnAsn.....AsnLysAspSerAsnPheGluAsnH 196
914 TTTACAGAGGCGATACACAT.....ACCGTCTNTTTTGAA 948
196 isPheArgGlyThrLeuAsnIleSerGlyLysValAspIleLeuMetGln 212
949 CCGCGCAGT.....AACGGACATTTTTCCTTTACATCCAACAACAA 989
213 AlaArgGlnGluAsnTrpAsnArgArgHisSerGlyArgSerHisTrpAs 229
990 CGGTACGGGTACGGTAACAGAAACCAACGAAAAGGTNTCCAATCCAAAGC 1039
229 nValThr.....ArgL 233
1040 TTAAAGTACAGACAGTCCGACTGTTTGACGAATCTTTGAATGAAACTGAT 1089
233 euAsnValSerThrAsnSerTyrLeuAsnIleThrIleAspAsnSerGly 249
1090 AAAGAACCAGTTTACGCGGCAGGGGGTGTTAATCAGTACCGTCCAAGGTT 1139
250 SerArgProSerProGlyAlaGlyProLeu.....TyrArgArgSerGl 264
1140 AAACAACGGT.....GAAAACCTTTCTTTTATCGATTACGGCAACG 1180
264 yLeuAsnGlyIleSerPheAsnAsnAspThrValPheAsnValAlaSerG 281
1181 GCAAACTCATC.....TTATCAAACAACATCAAC 1209
281 lySerAlaValAsnPheSerIleLysProProIleValSerAsnValHis 297
1210 CAAGGCGCGGGCGGTTTGTATTTTGAAGGTGATTTTACGGTCTCGCCTGA 1259
298 AspGlyAsnHisThrLeu...PheAsnGlyAsnValSerVal..... 310
1260 AAACAACGAAACGTGGCAAGGCGCGGGC.....GTTCATATCAGTG 1300
311 .....LeuGlyGlyGlyAspValAsnPheHisPheAsnA 322
1301 AAGACAGTACCGTTACTTGGAAAGTAAACGGCGTGGCAAACGACCGCCTG 1350
322 laSerSerSerAsnHisTrpThrHisGlyValValIleLysSerGlnAsn 338
1351 TCCAAAATCGGCAAAGGC...ACGCTGCACGTTCAAGCCAAAGGG..... 1392
339 PheAsnAlaSerGluGlySerSerLeuArgPheLysSerGluGlySerTh 355
1393 .....GAAAACCAAGGCTCGATCAGCGTGGGCGACG 1423
355 rArgThrAlaPheThrIleGluSerAspLeuThrLeuAsnAlaThrGlyG 372
1424 GTACAGTCATTTTGGATCAGCAGGCA.....GACGATAAAGGCAAAAAA 1467
372 lyAsnIleSerLeuAsnGlnValAlaGlyIleAspGlyAsnLeuGlnLys 388
1468 CAAGCCTTTAGTGAAATCGGCTTGNTCAGCGGCAGGGGTACGGTGCAACT 1517
389 SerLeuValAlaAsnLysAsnIleThrPheGluGlyGlyAsnIleThrLe 405
1518 GAATGCCGATAATCAGTTCAACCCCGACAAACTCTATTTCGGCTTTCGCG 1567
405 uAlaAla.....AspLysLysProIleGluIleLysG 416
1568 GCGGACGTTTGGATTTAAACGGGCATTCGCTTTCGTTCCACCGTATTCAA 1617
416 lyAsnIleThrValLysGluGlyAlaAsnValThrLeuArgSerAlaAsn 432
1618 ...AATACCGATGAAGGGGCGATGATTGNCNATCATAATGCCACAACAAC 1664
433 TyrGlyAsnAspLysSerAlaLeuSerIleArgGlyAsnValThrAsnLy 449
1665 ATCCACCGTTACCATTACAGGGAAT.....GAAAGTATTA 1699
449 sGlyAsnLeuThrValThrGlySerAlaIleAsnIleGluLysAsnLeuT 466
1700 CA...CAACCGAGTGGTAAGAATATCAATAGACTTAATTACAGCAAAGAA 1746
466 hrValGluGlySerAlaLysPheLeuAlaAsnProAsnTyrSerPheAsn 482
1747 ATTGCCTACAACGGTTGGTTTGGCGAG..... 1773
483 Val.....SerGlyLeuPheAspAsnGlnGlyLysSerAsnIleSerIl 497
1774 .....AAAGATACGACCAAAACGAACGGGCGGC 1801
497 eAlaLysGlyGlyAlaHisPheLysAspIleAsnAsnThrLysSer...L 513
1802 TCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCNGCTGCTTTCC 1851
513 euAsnIleThrThrAsnSerAspSerAlaTyrArgThrIleIleGluGly 529
1852 GGCGGAACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACTGTT 1901
530 AsnIleThrAsnSerAsnGlyAspLeuAsnIleThrAspAsnLys..... 544
1902 TTTCAGCGGCAGACCGACACCGCACGCCTACAATCATTTAGGAAGCGGGT 1951
545 .....AsnAsnAlaGluIleGlnIleGlyGlyAsnI 555
1952 GGTCAAAAATGGAAGGTATCCCACAAGGAGAAATCGTGTGGGACAACGAC 2001
555 leSerGlnLysGluGly..... 560
2002 TGGATCNACCGCACGTTTAAAGCGGAAAATTTCCATATTCAGGGCGGGCA 2051
561 .....AsnLeuThrIleSerSerAspLysIleAsnIleThr...AsnGl 574
2052 GGCGGTGATTTCCCGCAATGTTGCCAAAGTGGAAGGCGATTGNCATTTGA 2101
574 nIleThrIleLysLysGlyValAsnLysGluAspSerAspSerSerThrA 591
2102 GCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCATACA 2151
591 laAsnAsnAlaAsnLeu.....Thr 597
2152 ATCTGTACACGTTCGGACTGGACNGGTCTGACAAATTGTGTCGAANAAAN 2201
598 IleLysThrLys.....GluLeuGl 604
2202 CATTACCGACGATAAAGTGATTGCTTCATTGACTAAGACNGACNTNAGCG 2251
604 nLeuThrGlyAspLeuAsnIleSerGlyPheAspLysAlaGluIleThrA 621
2252 GCANTGTNAGNCTNNCCNATNACGNTNNTTNAAANCTCNCNGGGCNTGCN 2301
621 laLys.....GluGlyAlaAsp 626
2302 NCACTNAANGGCAATCTTAGTGCAAATGGC..... 2331
627 LeuIleIleGlyAsnSerAspAsnAsnAsnAsnAlaAsnAlaLysLysVa 643
2332 .....GATACACGTTATACAGTC...AGCCACAACG 2359
643 lThrPheAsnGlnValLysAspSerLysIleSerAlaAspSerHisAsnV 660

```
2360 CCACCCAAAACGGCAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATTT 2409
     ::|||   |||::::::::::::
 660 alThrLeuAsnSerLysValGlu..................................... 667

2410 AATCAAGCCACATTAAACGGCAACNCATCGGNTTCGGGCAAT........ 2451
              |||   |||||||||   ::::::::::::|||
 668 .........ThrSerAsnGlyAsnAsnAspAlaGluSerAsnAsnGlyAs 681

2452 ..........GCTTCATTTAATCTAAGCAACAACGCCGCACAAAACGGC. 2490
                    ::::::|||   :::|||   ::::::::::|||:::
 681 pGlyThrSerLeuThrIleAsnAlaLysAsnIleThrValAsnAsnAsnI 698

2491 ....................AGTCTGACGCTTTCCGACAAC......GCT 2514
                         :::::::|||   |||:::|||      :::
 698 leThrSerHisLysThrValAsnIleThrAlaSerGluAsnValThrThr 714

2515 AAGGCAAACGTAAGCCATTCCGCACTCAACGGCAATGTCTCCCTAGCCGA 2564
     ||||||:::::::::   :::|||   :::|||:::|||::::::::::
 715 LysAlaGlyThrThrIleAsnAlaThrThrGlySerValGluValThrAl 731

2565 TAAGGCAGTATTCCATTTTGAAAACAGCCGCTTTACCGGACAACTCAGCG 2614
       |||                                 ||||||::::::::::|
 731 aLys.............................ThrGlyAspIleLysG 738

2615 GCAGCAAGGANACAGCATTACACTTAAAAGACAGCGAATGGACGCTGCCG 2664
     ||:::            ::::::      :::::::::   ||||||
 738 lyLys............ValGluSerThrSerGlySerValThrLeuThr 750

2665 TCAGGCACGGAA.........TTAGGCAATTTAAACCTTGACAACGCCAC 2705
     :::      |||         :::::::|||::::::   ::::::::::||
 751 AlaThrGlyGluAlaLeuAlaValSerAsnIleSerGlyAsnThrValTh 767

2706 CATTACACTCAAT.................................T 2719
     |||||||   |||                                 |
 767 rIleThrAlaAsnLysGlyLysLeuThrThrGlnAlaGlySerThrValS 784

2720 CCGCCTATCGCCACGATGCTGCAGGCGCGCAAACCGGCAGNGTGTCAGAC 2769
     |||||   :::      :::|||::::::|||:::|||   :::|||
 784 erAlaIleAsnGlyValThrAlaSerSerGlnSerGlyAspIleSerGly 800

2770 ACGCCGCGCCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAAC 2819
     |||                                  ::::::   :: ||
 801 Thr..............................IleSerGlyAsnTh 806

2820 TTCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACN 2869
     |         |||   ::::::   ||||||::::::::
 806 rValLysValSerAlaIleGlyAspLeuThrThrLysSerGly..... 820

2870 GTCAAGGAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGAAGCGAC 2919
                          |||||||:::
 821 ......................SerGluIle................. 823

2920 AAATTGAAGCTGGCGGAA............AGTTCCGAAGGNACTTAC.. 2955
     |||   |||   :::|||           |||:::   ||||||
 824 LysAlaLysThrGlyGluAlaAsnValThrSerAlaThrGlyThrIleGl 840

2956 ....ACCTTG.........GCGGTCAAC.........AATACCGGCAAC. 2982
         |||:::         |||||||||         |||||||||:::
 840 yGlyThrIleSerGlyAsnAlaValAsnValThrAlaAsnThrGlyAspL 857

2983 ...........GAACCCGTAAGCCTCGAT.................CAA 3003
                :::   ::::::::::|||
 857 euThrValGluAspAlaAlaLysIleAspAlaThrGlyGlyAlaAlaThr 873

3004 TTGACGGTAGTGGAAGGGAAAGACAACAAACCGCTGTCCGAAAACCTTAA 3053
     ||||||:::::: :::|||||||   |||:::::::::   :::::::::
 874 LeuThrAlaThr.SerGlyLysLeuThrThrLysAlaSerSerSerIleT 890

3054 TTTCACCCTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTACCAAC 3103
       |||                                 |||::::::   :::|||
 890 hrSer.........................AlaAsnAsnGlnValAsn 897

3104 TCATCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAA 3153
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          |||||||||   :::|||   :::      |||::::::   |||
 898 LeuSerAlaLysAspGlySerIleGlyGlyAsnIleAsnAlaAlaAsnVa 914

3154 GAGCTTTCCGACAAACTCGGCA 3175
        ::::::   |||:::::::|||
 914 lThrLeuAsnThrThrGlyAla 921
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seq_documentation_block:

ID AAW04505 standard; Protein; 1992 AA.
XX
AC AAW04505;
XX
DT 25-JAN-1997 (first entry)
XX
DE Moraxella 200 kDa outer membrane protein.
XX
KW Outer membrane protein; OMP; immunogen; vaccine; otitis media;
KW diagnosis.
XX
OS Mycobacterium catarrhalis strain 4223.
XX
PN WO9634960-A1.
XX
PD 07-NOV-1996.
XX
PF 29-APR-1996; 96WO-CA00264.
XX
PR 26-MAR-1996; 96US-0621944.
PR 01-MAY-1995; 95US-0431718.
PR 07-JUN-1995; 95US-0478370.
XX
PA (CONN-) CONNAUGHT LAB LTD.
XX
PI Chong P, Harkness RE, Klein MH, Loosmore SM, Sasaki K;
XX
DR WPI; 1996-506162/50.
DR N-PSDB; AAT38740.
XX
PT Moraxella outer membrane protein - useful as immunogen in protective
PT vaccine and for diagnosis
XX
PS Claim 14; Fig 6; 109pp; English.
XX
CC An approx. 200 kDa outer membrane protein (AAW04505) can be
CC isolated from Moraxella catarrhalis otitis media strain 4223
CC by electroelution, or expressed from a gene (see also AAT38740)
CC obtd. from a strain 4223 genomic library. Natural or recombinant
CC outer membrane protein is useful as an immunogen to protect
CC against infection by Moraxella, esp. M. catarrhalis. It can
CC also be used to detect antibodies, esp. for differential diagnosis
CC between bacteria that cause similar symptoms, and also useful as
CC a carrier for other antigens and used to raise antitumour
CC antibodies for conjugation to therapeutic agents.
XX
SQ Sequence 1992 AA;

alignment_scores:

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              Ratio:  0.316                 Gaps:     72
 Percent Similarity:  44.102   Percent Identity: 18.391
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alignment_block:

US-09-303-518D-651 x AAW04505 ..

Align seg 1/1 to: AAW04505 from: 1 to: 1992

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     163 CGCGACTTTGCCGAAAATAAAGGCAAGTTTGCAGTC.....GG 200
         ::|||   :::::::|||   |||      ::::::        ||
     602 LysAspThrThrLysAsnAlaGlyAlaValSerIleLeuLysLeuLysGl 618
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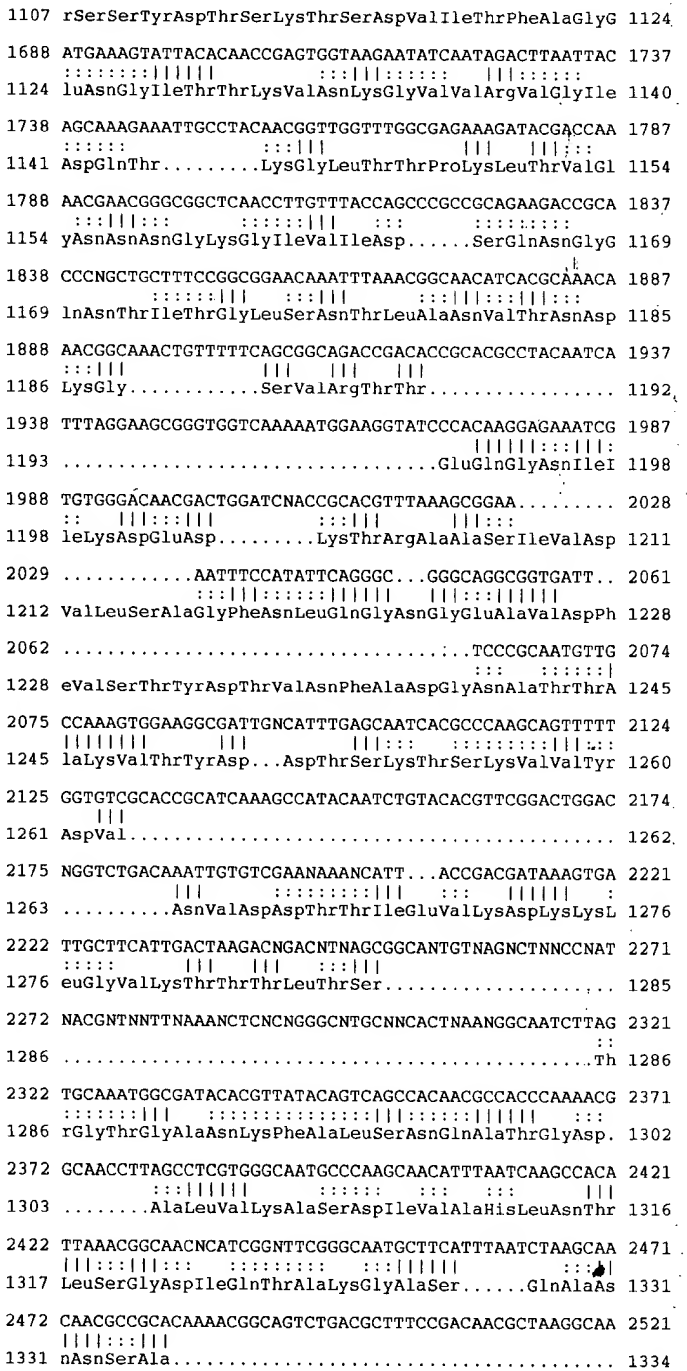
1107 rSerSerTyrAspThrSerLysThrSerAspValIleThrPheAlaGlyG 1124
1688 ATGAAAGTATTACACAACCGAGTGGTAAGAATATCAATAGACTTAATTAC 1737
1124 luAsnGlyIleThrThrLysValAsnLysGlyValValArgValGlyIle 1140
1738 AGCAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACCAA 1787
1141 AspGlnThr.....LysGlyLeuThrThrProLysLeuThrValGl 1154
1788 AACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCA 1837
1154 yAsnAsnAsnGlyLysGlyIleValIleAsp.....SerGlnAsnGlyG 1169
1838 CCCNGCTGCTTTCCGGCGGAACAAATTTAAACGGCAACATCACGCAAACA 1887
1169 lnAsnThrIleThrGlyLeuSerAsnThrLeuAlaAsnValThrAsnAsp 1185
1888 AACGGCAAACTGTTTTTCAGCGGCAGACCGACACCGCACGCCTACAATCA 1937
1186 LysGly.....SerValArgThrThr..... 1192
1938 TTTAGGAAGCGGGTGGTCAAAAATGGAAGGTATCCCACAAGGAGAAATCG 1987
1193 .....GluGlnGlyAsnIleI 1198
1988 TGTGGGACAACGACTGGATCNACCGCACGTTTAAAGCGGAA..... 2028
1198 leLysAspGluAsp.....LysThrArgAlaAlaSerIleValAsp 1211
2029 .....AATTTCCATATTCAGGGC...GGGCAGGCGGTGATT.. 2061
1212 ValLeuSerAlaGlyPheAsnLeuGlnGlyAsnGlyGluAlaValAspPh 1228
2062 .....TCCCGCAATGTTG 2074
1228 eValSerThrTyrAspThrValAsnPheAlaAspGlyAsnAlaThrThrA 1245
2075 CCAAAGTGGAAGGCGATTGNCATTTGAGCAATCACGCCCAAGCAGTTTTT 2124
1245 laLysValThrTyrAsp...AspThrSerLysThrSerLysValValTyr 1260
2125 GGTGTCGCACCGCATCAAAGCCATACAATCTGTACACGTTCGGACTGGAC 2174
1261 AspVal..... 1262
2175 NGGTCTGACAAATTGTGTCGAANAAANCATT...ACCGACGATAAAGTGA 2221
1263 .....AsnValAspAspThrThrIleGluValLysAspLysLysL 1276
2222 TTGCTTCATTGACTAAGACNGACNTNAGCGGCANTGTNAGNCTNNCCNAT 2271
1276 euGlyValLysThrThrThrLeuThrSer..... 1285
2272 NACGNTNNTTNAAANCTCNCNGGGCNTGCNNCACTNAANGGCAATCTTAG 2321
1286 .....Th 1286
2322 TGCAAATGGCGATACACGTTATACAGTCAGCCACAACGCCACCCAAAACG 2371
1286 rGlyThrGlyAlaAsnLysPheAlaLeuSerAsnGlnAlaThrGlyAsp. 1302
2372 GCAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATTTAATCAAGCCACA 2421
1303 .....AlaLeuValLysAlaSerAspIleValAlaHisLeuAsnThr 1316
2422 TTAAACGGCAACNCATCGGNTTCGGGCAATGCTTCATTTAATCTAAGCAA 2471
1317 LeuSerGlyAspIleGlnThrAlaLysGlyAlaSer.....GlnAlaAs 1331
2472 CAACGCCGCACAAAACGGCAGTCTGACGCTTTCCGACAACGCTAAGGCAA 2521
1331 nAsnSerAla..... 1334
2522 ACGTAAGCCATTCCGCACTCAACGGCAATGTCTCCCTAGCCGATAAGGCA 2571
1335 .....GlyTyrValAspAlaAspGlyAsnLysValIleTyrAspSerThr 1349
2572 GTATTCCATTTTGAAAACAGCCGCTTTACCGGACAACTCAGCGGCAGCAA 2621
1350 AspAsnLysTyrTyrGlnAlaLysAsnAspGlyThrValAspLysThrLy 1366
2622 GGANACAGCATTACACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCA 2671
1366 sGluValAlaLysAspLysLeuValAlaGlnAlaGlnThrProAspGlyT 1383
2672 CGGAATTAGGCAATTTAAACCTTGACAACGCCACCATTACACTCAATTCC 2721
1383 hr...LeuAlaGlnMetAsnValLysSer.....ValIleAsnLys 1395
2722 GCCTATCGCCACGATGCTGCAGGCGCGCAA..... 2751
1396 GluGlnValAsnAspAlaAsnLysLysGlnGlyIleAsnGluAspAsnAl 1412
2752 .....ACCGGCAGNGTGTCAGACACGCCGCGCCGCCGTT 2785
1412 aPheValLysGlyLeuGluLysAlaAlaSerAspAsnLysThrLysAsnA 1429
2786 CGCGCCGTTCCCTA.....TTATCCGTTACACCGCCAACTTCGGTAGAA 2829
1429 laAlaValThrValGlyAspLeuAsnAlaValAlaGlnThrProLeuThr 1445
2830 TCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACNGTCAAGGAAC 2879
1446 PheAlaGlyAspThrGlyThrThrAlaLysLysLeuGlyGluThrLeuTh 1462
2880 ATTCCGCTTTATGTCGGAACTCTTCGGCTACCGAAGCGACAAATTGAAGC 2929
1462 rIleLys.....GlyGlyGlnThrAspThrAsnLysL 1473
2930 TGGCGGAAAGTTCCGAAGGNACTTACACCTTGGCGGTCAACAATACCGGC 2979
1473 euThrAspAsnAsnIleGlyValVal..... 1481
2980 AACGAACCCGTAAGCCTCGATCAATTGACGGTAGTGGAAGGGAAAGACAA 3029
1482 .....AlaGlyThrAspGlyPheThrValLysLeuAlaLysAsp.. 1494
3030 CAAACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAACACGTCG 3079
1495 .....LeuThrAsnLeuAsn.....SerValA 1502
3080 ATGCCGGCGCGTGGCGT.....TACCAACTCATCCGCAAA 3114
1502 snAlaGlyGlyThrLysIleAspAspLysGlyValSerPheValAspSer 1518
3115 GACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGA 3164
1519 SerGlyGlnAlaLysAlaAsnThrProValLeuSerAlaAsnGlyLeuAs 1535
3165 CAAACTCGGCAAG.....GCAGAAGCCAAAAAACAGGCGG 3199
1535 pLeuGlyGlyLysValIleSerAsnValGlyLysGlyThrLysAspThrA 1552
3200 AAAAAGACAACGCGCAAAGCCTTGAC.....GCGCTG 3231
1552 spAlaAlaAsnValGlnGlnLeuAsnGluValArgAsnLeuLeuGlyLeu 1568
3232 ATTGCGGCCGGGCGCGATGCCGCCGAAAAGACAGAA.....AG 3269
1569 GlyAsnAlaGlyAsnAspAsnAlaAspGlyAsnGlnValAsnIleAlaAs 1585
3270 CGTTGCCGAACCGGCCCGGCNGGCAGGCGGGGAAAATGTCGGCATTATGC 3319
1585 pIleLysLysAspProAsnSerGlySerSerSerAsnArgThrValIleL 1602

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3320 AGGCG............................GAGGAAGAGAAAAAA 3339
     ::|||                           :::   ||||||
1602 ysAlaGlyThrValLeuGlyGlyLysGlyAsnAsnAspThrGluLysLeu 1618

3340 ..............CGGGTGCAGGCGGATAAAGACAGCGCNTTGGCGAA 3374
                  :::|||   :::|||||||||:::
1619 AlaThrGlyGlyIleGlnValGlyValAspLysAspGly........... 1631

3375 ACAGCGCGAAGCGGAAACCCGGCCGGNTACCACCGCCTTCCCCCGCGCCC 3424

1631 ................................................. 1631

3425 GCNGCGCCCGCCGGGATTTGCCGCAACCGCAGCCCCAACCGCAACCTCAA 3474
       |||:::  ||||||  :::       :::  |||  :::
1632 ..AsnAlaAsnGlyAspLeuSerAsnValTrpValLysThrGln...Lys 1646

3475 CCCCAACCGCAGCGCGACCTGATNAGCCGTTATGCCAATAGCGGTTTGAG 3524
           ::::::  |||  :::  |||     :::|||  ::
1647 AspGlySerLysLysAlaLeuLeuAlaThrTyrAsnAlaAlaGlyGlnTh 1663

3525 TGAATTTTCCGCCACGCTCAACAGCGTTTTCGCCGTACAGGACGAATTGG 3574
     :::::::     |||  |||  :::  |||:::             |
1663 rAsnTyr...LeuThrAsnAsnProAlaGluAlaIle.........A 1675

3575 ACCGCGTGTTTGCCGAA.............................. 3591
     |||||:::     :::
1675 spArgIleAsnGluGlnGlyIleArgPhePheHisValAsnAspGlyAsn 1691

3592 ..............GACCGCCGCAACGCNGTTTGGACAAGCNGCATCCG 3626
                  :::  ||||||::::::  :::|||:::
1692 GlnGluProValValGlnGlyArgAsnGlyIleAspSerSerAla..... 1706

3627 GNACACCAAACACTACCGTTCGCAAGATTTCCGCGCCTACCGCCAACAAA 3676
      :::  ||||||     :::     |||:::|||     :::
1707 .SerGlyLysHisSerValAlaIleGlyPheGlnAlaLysAlaAspGlyG 1723

3677 CCGACCTGCGCCAAATCGGTATGCAGAAAAACCTCGGCAGCGGGCGCGTC 3726
                 ||||||  |||  :::  |||:::     :::
1723 luAlaAlaValAlaIleGlyArgGlnThrGlnAlaGlyAsnGlnSerIle 1739

3727 GGCATCCTGTTTTCGCACAACCGGACC...GAAAACANCTTCGACGACGG 3773
     :::|||     :::  :::  |||  ::::::::::::     ||
1740 AlaIleGlyAspAsnAlaGlnAlaThrGlyAspGlnSerIleAlaIleGl 1756

3774 CATCGGCAACTCGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAATACG 3823
     |  ||||||  :::        |||::::::::::::|||:::'  :
1756 yThrGlyAsnValValAlaGlyLysHisSerGlyAlaIleGlyAspProS 1773

3824 GCATCGGCAGGTTCGACATCGGCATCAGCACGGGCGCGGGT......TTT 3867
     ::      :::  |||  :::  |||:::|||  :::     |||
1773 erThrValLysAlaAspAsnSerTyrSerValGlyAsnAsnAsnGlnPhe 1789

3868 AGCAGCGGCANTCTNTCAGAC......GGCATCGGAGGCAAAATCCGC.. 3909
     ::::::::::::  :::|||     |||:::|||:::::::|||
1790 ThrAspAlaThrGlnThrAspValPheGlyValGlyAsnAsnIleThrVa 1806

3910 ........................................CGCCGCG 3916

1806 lThrGluSerAsnSerValAlaLeuGlySerAsnSerAlaIleSerAlaG 1823

3917 TGCTGCATTACGGCATTCAGGCACGATACCGCGCCGGTTTCGGC...... 3960
          |||  |||  ||||||:::         |||  :::
1823 lyThrHisAlaGlyThrGlnAlaLysLysSerAspGlyThrAlaGlyThr 1839

3961 ..............................GGATTCGGCATCGAACC 3977
                                    ||||||:::  :::
1840 ThrThrThrAlaGlyAlaThrGlyThrValLysGlyPheAlaGlyGlnTh 1856

3978 GTACATCGGCGCAACGCGCTATTTCGTCCAAAAAGCGGATTACCGCTACG 4027
       :::||||||:::        ::::::  |||:::  |||  :
1856 rAlaValGlyAlaValSerValGlyAlaSerGlyAlaGluArgArgIleG 1873

4028 AAAACGTCAATATC................................ 4041
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     ::||||||
1873 lnAsnValAlaAlaGlyGluValSerAlaThrSerThrAspAlaValAsn 1889

4042 ....................................GCCACCCCCGG 4052
                                        ||||||
1890 GlySerGlnLeuTyrLysAlaThrGlnSerIleAlaAsnAlaThrAsnGl 1906

4053 TCTTGCGTTCAACCGNTACCGNGCGGGCATTAAGGCAGATTATTCATTCA 4102
      |||      :::   ::::::        |||||||:::   :::::::
1906 uLeuAspHisArgIleHisGlnAsnGluAsnLysAlaAsnAlaGlyIleS 1923

4103 AACCGGCGCAACACATNTCCATCACNCCTTATTTNAGCCTGTCCTATACC 4152
     ::   |||:::      :::      |||  :::  :::
1923 erSerAlaMetAlaMetAlaSerMetProGlnAlaTyrIleProGlyArg 1939

4153 GATGCCGCTTCGGGCAAAGTCCGAACACGCGTCAATACCGCNGTATTGGC 4202
     :::  ::::::|||  :::  |||:::  :::  :::::::::||
1940 SerMetValThrGlyGlyIleAlaThrHisAsnGlyGlnGlyAlaValAl 1956

4203 TCAGGATTTCGGCAAA...ACCCGCAGTGCGGAATGG...........G 4237
     |      ::::::|||  :::  :::::::::|||           :
1956 aValGlyLeuSerLysLeuSerAspAsnGlyGlnTrpValPheLysIleA 1973

4238 GCGTAAACGCCGAAATCAAAGGTTTCACGCTGTCCNTCCACGCTGCCGCC 4287
     ::  :::|||:::  :::|||              |||::::::|||
1973 snGlySerAlaAspThrGlnGly.............HisValGlyAla 1984

4288 GCCAAAGGN 4296
     |||  |||
1985 AlaValGly 1987
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